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BRITISH MEDICAL JOURNAL

LONDON SATURDAY MARCH 14 1953

OPPORTUNITIES FOR RESEARCH IN GENERAL PRACTICE*

BY

ROBERT PLATT, M.D., M.Sc., F.R.C.P.

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It has always seemed to me a pity that our three leading medical journals which deal with general medical topics as opposed to specialties—namely, the *British Medical Journal*, the *Lancet*, and the *Practitioner*—contain so few articles by general practitioners. It has also seemed to me a pity that those who have facilities for research usually have little access to, or little interest in, the common afflictions of the people, whereas those who have access to and experience of the common afflictions have little time or opportunity to study them.

An Attitude of Mind

To some extent this is both the result of, and responsible for, certain common misconceptions about research. The conventional picture of the research worker is that of a rather austere man in a white coat with a background of complicated glassware. My idea of a research worker, on the other hand, is a man who brushes his teeth on the left side of his mouth only so as to use the other side as a control and see if tooth-brushing has any effect on the incidence of caries. In other words, I am speaking of research not as a career but as an attitude of mind.

Anyone who has to read, as I have, many medical papers which are rejected, as well as many which are published, must realize that a number of people doing research at the present time have little aptitude for it, being sterile of ideas and lacking in the simplicity of approach to a problem which is so often the mark of a good piece of work. The idea of " doing some research " has come first, the finding of a problem second. Ideally it should be the other way round, though I admit that one must first get rid of the misconception that research can be done only by people specially paid and equipped to do it.

When doctors come to ask, as they occasionally do, whether they could work towards an M.D. thesis, this wrong attitude to research is frequently displayed. Research, to their minds, means doing some laboratory test, so they have thought out some slight modification of some simple test which they contemplate trying out in 100 patients ; for instance, doing sedimentation rates on people with migraine. Now, this type of thing is rarely worth doing at all, and, if it is, it could be done better in a hospital by technicians than in general practice. Far better as a research worker is the man who cleans his teeth only on the left side. He has a problem to solve, and an important one, and a simple way to solve it. If he has been badly educated in elementary principles he might clean only his top teeth and not the bottom ones ; but that would admit a possible error of selection, for the top and bottom sets, being morphologically different, may differ inherently in their resistance to disease. If he is a really good worker, on the other hand, he will urge his brother—preferably an identical twin—to clean only the right side and compare results. You may well ask why I have not made this simple experiment myself. The answer is that when the idea arose recently out of a conversation with Dr. Margaret Roscoe in my department it was already too late.

A Wartime Experience

Before going further I would like to speak of an experience which I think illustrates some of the points that I wish to make. Towards the end of the Tunisian campaign, about April or May of 1943, I was in a general hospital very near to Tunis. When the epidemic of bacillary dysentery broke out with sudden violence among British, Free French, American, German, and Italian soldiers alike, we were of course immediately flooded with cases. Practically the whole hospital became medical and practically every ward became a dysentery ward. We had no nurses or sisters, only nursing orderlies, many of whom had had the scantiest of training. The hospital had been hurriedly erected, conditions were extremely primitive, flies were so prevalent that you ate your food with one hand while flicking off the flies with the other. Many of our medical officers themselves developed dysentery, and those who remained on duty were therefore grossly overworked. Sulphaguanidine was new and was in short supply, so that we could not use it for more than about a third of our cases. These seemed to me to be ideal conditions for a bit of research, for I had long wondered if the traditional treatment of dysentery by sodium and magnesium sulphate had any advantage over simple rest in bed and a fluid diet.

Conditions were ideal for four reasons. First, the number of cases likely to be treated personally in the next few weeks was going to be very large, and therefore statistically significant results would be obtained. Secondly, since the evidence would all be compiled in one epidemic it would eliminate errors due to treating cases at different times and under variable climatic

*An address given to the Section of General Practice of the Manchester Medical Society on October 27, 1952.

and geographical conditions. Thirdly, sulphaguanidine, which was likely to prove very beneficial, was in short supply and so no ethical problem arose of the justification for withholding it from one batch of cases. Finally, the population to be studied, being a military one, did not show the variations in age, sex, and occupation usual in civilian practice.

The sergeant dispenser was instructed to make up a special dysentery medicine, which was in fact a placebo containing colouring and flavouring matter. Patients were divided into three groups. One group had sodium sulphate, another had the special mixture, and the third had sulphaguanidine. Cases were unselected, and were put into groups according to their order of admission, with the exception that any case whose illness was deemed to be unusually severe or dangerous was put into the sulphaguanidine group. Since this group was likely to behave best, this acknowledged error of selection would weight the evidence in a direction unfavourable to the probable result, and so was permissible. This part of the planning took perhaps half an hour. It remained to decide what were the simplest criteria on which to judge results with the minimum of time consumption—for instance, diarrhoea, blood in the stools, pyrexia, and so on. But as one would not allow a man to get up from bed until blood in the stools, gross diarrhoea, and pyrexia had ceased, it was really enough to take the time from admission to hospital as a fresh case (not a transfer) until the patient was allowed to get up. To note this in a book in which the three groups were recorded, without respect to name, rank, or age, was therefore all that was necessary.

The answer was clear-cut. Sodium sulphate was no better than the placebo treatment, if as good; but the sulphaguanidine group fared much better than either of the others in spite of being unfavourably loaded by containing the more severe cases.

Making Use of Opportunity

Now, I quote this in the first place to take the wind right out of the sails of those who say they have no time to do research; secondly, to show the importance of planning in advance; and thirdly, to show the importance of making use of opportunities.

There may be some who think that giving sulphonamides early in influenza prevents complications and shortens the illness. It could be proved one way or another in the next influenza epidemic if plans were ready. No hospital in the country can do it. Of course, in general practice, with patients varying widely in age, it would probably be necessary to take account of age and sex, but the patient's card would give this information and you need only put down S for sulphonamide case, A for aspirin, if that is going to be the alternative, and a number to represent days in bed, and another number to represent days off work. Treat cases alternately with one method or the other, and when the epidemic is over and there is an hour or two to spare add up the figures and publish the results. They might save the country thousands of pounds in sulphonamides or, alternatively, thousands of man-hours by returning workers earlier to their occupations. Of course, as in all experiments, something quite unpredicted might come out. Careful analysis might show, for instance, that, whereas in nine cases out of ten the alternative drugs made no difference, there was a small group which did particularly well (or badly) on sulphonamides. This might lead to further research to see what were the factors involved in this unexpected result. In this way one becomes led on from one problem to another, and perhaps only rarely ends by discovering what one set out to find.

The Statistical Method

Research is worth doing even if the results are never published; it gives personal satisfaction and makes work more interesting, more accurate, and more efficient. Research on common diseases in general practice could be of at least two kinds—the short-term acute research such as that outlined, or the long-term one. Both need planning in advance. In the short-term experiment one would choose an epidemic in which there would be enough cases for statistical analysis to be relatively unimportant. In a long-term experiment statistics would have to be considered from the beginning. Statistics is a subject about which people have views or by which they may be frightened, and it is not unusual for them to conceal their fear beneath a bold contempt. "Statistics can prove nothing," and, "Statistics can prove anything," are the two opposing statements often uttered. Statisticians don't attempt to prove anything. They merely apply a mathematical test to the results which will tell whether they are likely to have occurred by chance or whether they are much more likely to be explained by some real difference of circumstance between the groups being compared.

A good deal of the research which could be done in general practice is bound to be statistical in nature, though that does not imply that you need to be a statistician to engage in it. Much of what statistics can show is common sense and is obvious to any critical worker, but a grasp of the first principles of statistical method will often avoid falling into a number of errors and fallacies, and it is nowadays fairly easy to obtain help from an elementary textbook or from someone statistically minded, when necessary. Clinical research often consists in the comparison of one group of cases with another group of cases differently treated, as in the influenza and dysentery examples, or the comparison may be made between the group studied and the known behaviour of the illness under consideration. For instance, if you have a new way of managing cases of coronary occlusion which you hope will reduce the mortality, you can either treat alternate cases and compare the treated with the control group, or you can, in an instance such as this, treat all cases and compare the results with the known mortality from coronary occlusion in series of cases published by other authors. Of course research need not be therapeutic; the incidence of osteoarthritis in heavy workers might be compared with the incidence in sedentary workers or in the population at large.

Value of Statistics

The statistical side of the problem should usually have some consideration before an experiment is started. Suppose the mortality from coronary occlusion in cases not immediately fatal (obviously these would have to be excluded as they could not be treated) is known to be 25%. Suppose you treat ten cases and all but one recover, your mortality therefore is 10%, whereas the general mortality is 25%. This may seem convincing, but statistics will tell you that it could happen in about one in four of such trials by pure chance. It is in fact a good deal more likely than picking up a bridge hand with two aces in it (which happens about once in five hands), and no one would consider that worth writing to the *B.M.J.* about. Statistics can tell you that if your results show a 10% mortality and the general death rate is 25% you would need to have about 35 or more cases for the results to be significant. What we term statistically significant is a purely arbitrary standard, the usual one accepted being that the result would occur by chance less than once in twenty trials. If you need 35 cases to make the results above the likelihood of chance, and you see only about five cases of coronary occlusion annually, obviously this bit of research is going to take seven years. Surely this is a piece of information worth knowing.

It is quite true that statistics can prove nothing. The fact that results are not significant does not mean that your

new treatment is no use; it may be, or it may not, and if the trend is in the right direction it is worth while to continue and to record a larger series. On the other hand, if the results *are* significant statistically it does not prove that it is your treatment which is making the difference. It still might be due to chance, though that is unlikely, or it may be due to other factors which have not been controlled. Here we come to what statisticians call errors of sampling. If you are to compare one group of cases with another, it is essential that, so far as is possible, they should be the same in all respects except for the difference which is being studied.

A paper which I had to read recently gave the ratio of male to female cases in a certain type of cancer as about 5 to 2. The ratio was compiled from about 60 post-mortem examinations and would therefore appear to be significant, but the author omitted an essential piece of information—namely, the sex ratio of all post-mortem examinations over the same period of time at that hospital. For the hospital might contain far more male than female beds, or, alternatively, the house-physician might have found it much easier to obtain permission for necropsy on his male patients. For reasons of this kind it is often much more difficult to do clinical research in hospitals, especially in very specialized ones, where patients are highly selected before ever being sent to hospital; and there are undoubtedly many problems, as we shall see later, which can be solved only in general practice. But even in general practice errors of selection or sampling are bound to occur, and one must always be on the lookout for them. It would, for instance, be unwise to come to any conclusion on dietetic habits of the population if your practice is largely confined either to the well-to-do or to those in the lower-income groups.

In any case, results must be interpreted with full allowance for all the possible factors involved irrespective of their statistical significance, and, especially in writing up the results for publication, it is most important to separate fact from inference. It may be a fact that one group of patients has recovered more quickly than another; as to what are the causes of the difference is for you or for others in full knowledge of the circumstances to infer. Obviously the inference may be wrong even though the facts are incontestable.

Some Suggestions

That is all I want to say on methods; now for a few suggestions on subjects for research which might be studied in general practice—many of them could be studied only in general practice. Subjects which should be suitable are the incidence of certain common disorders in the population—what proportion of people suffer from migraine, for instance; the influence of occupation, social conditions, and heredity upon common ailments; and the treatment of complaints, including neuroses. Here are a few specific suggestions. I have often been impressed by the frequency with which patients with hypertension will give a history of having had migraine in the past. Whether this is pure coincidence because hypertension and migraine are both common disorders, or whether the two complaints are related, or whether hypertension is more likely to be discovered because the patient complains of migraine, I do not know, nor can I find out, for the people I see are highly selected, usually because of the severity of their complaint or because of its resistance to treatment. If we knew the incidence of migraine in the general population of persons who visit doctors, and in the hypertensive population, or if we knew what percentage of sufferers from migraine had blood pressure above the average, we would have the answer.

Physicians, having seen a case of effort syndrome or aerophagy, for instance, after taking reasonable precautions to exclude organic disease, usually recommend explanation and reassurance. Does it do any good? What are the results of a follow-up of such patients when half have been treated by simple psychotherapy and the other half by bottles of medicine for indigestion or palpitation?

Rheumatic complaints: how many fit into a recognized pattern such as osteoarthritis, rheumatoid arthritis, displaced disks, occupational strains, and neuroses? How many are left which cannot be so classified? Is there such a disease as fibrositis? In questions such as these some radiological and other expert help may be required, but there is little doubt that it would be forthcoming if the case were sent for a hospital consultation where necessary, so long as the requests were reasonable.

It is well recognized that an important cause of hypertension and of renal failure is pyelonephritis. In hospital we see only the cases that go wrong, and they are probably only a small minority. What percentage of patients who have a urinary infection later develop these complications? Again it is a question which can be answered only by general practitioners. Perhaps the cases in any one practice would be too few to give the answer in a reasonable time; if so, several doctors could combine to make a survey of their patients. This type of research would certainly need a little extra work, but not necessarily very much. It might be done by confining one's interest from a research point of view strictly to the one subject. It is rarely possible to be investigating two subjects at the same time. In all cases of cystitis or pyelonephritis the blood pressure would be recorded and the urine would be examined for pus cells as a rough confirmation of the diagnosis. A special mark would then be put on the patient's card. This might, I suppose, mean an extra twenty minutes' work every few weeks. In times of stress cases might have to be omitted from the series. In a few years' time an effort would be made to re-examine all the cases in which a urinary infection and blood-pressure reading had been recorded.

Sciatica is another subject for research. The orthopaedic surgeons in hospital practice see only a highly selected population and are in danger of assuming that all cases of sciatica require a laminectomy. But I seem to remember that before displaced disks were recognized one did not see a large proportion of the population hobbling about with incurable sciatica. What proportion of cases recover quite quickly with simple conservative treatment? Again it is a problem which can be answered only by general practitioners.

Do people with a tendency to obesity have a predilection for certain foods? Would it be worth while preparing a list of foods, including delicacies such as cream buns, and asking thin and fat patients to mark honestly the foods which they like very much, like fairly well, tolerate, or avoid? Speaking of obesity, I commend the article by Edwards and Swyer (1950) to all practitioners. These authors, by a very simple piece of research which could easily have been done in general practice (but was not), showed that dextroamphetamine had a highly significant effect as an adjunct to a low-calorie diet, whereas thyroid extract, which had been used for many years, had none at all.

Does having baths have any bearing on the liability to skin complaints? Will frequent scrubbing of the fingernails prevent the spread of boils? Does a furred tongue indicate any recognizable state of health or is it associated with dietetic fads? Are cough medicines other than sedatives any use? Or would the chronic bronchitic be just as satisfied with gentian and soda?

Therapeutic Experiments

In questions of therapy, ethical considerations may arise. Obviously it would not be right, for instance, to withhold penicillin from cases in which its efficacy is already proved, but many of the common minor ailments are either trivial or self-limiting, or are known to be little influenced by treatment.

Professor Pickering once remarked that doctors are really experimenting every day. Every time a prescription for sulphonamides is written an experiment is started, and one not free from danger. An effort is being made to find out

whether the patient's illness will respond or not. The trouble is that most of the experiments are bad ones; they almost seem to be designed to perpetuate ignorance instead of to give the answer to a question. I would only ask that the experiments should be designed a little more logically to find the answers. This is the real essence of research, which, as I have said, is an attitude of mind. It is an attitude of mind which is not taken in by custom, prejudice, or false logic, but which seeks to find an answer. Those who are disinclined to depart from custom might remember that the man who first gave up the practice of blood-letting departed from the custom of his day. No one would doubt that he was a benefactor to mankind.

An example of a good therapeutic experiment came to my notice a little while ago. My friend Dr. Peter Duncan is interested in lymphocytic choriomeningitis. A case was admitted to hospital which he had reason to believe (and later proved) to be in the pre-meningitic stage of this disease. There is some doubt about whether it responds to aureomycin. Duncan thinks that it does not, and that others who claim benefit from its use have given aureomycin at the stage when the second (meningitic) temperature peak is about to run its natural course towards resolution. He therefore gave this man aureomycin in full doses in the pre-meningitic phase, and proved that, so far from having an effect, it was powerless to prevent the second rise of temperature and the onset of meningitic symptoms. Thus by giving an expensive drug which he believed to be useless, in such a way that its value, if any, could be assessed, he proved his point, and at the expense of a few pounds may have saved hundreds of other cases from being treated in the same useless manner. I know that one case is not proof, but in an experiment as well designed as this one it is very strong evidence. Moreover, choriomeningitis is a fairly uncommon disease, but I am sure that if practitioners cared to make a few properly recorded critical experiments of this kind they could be the means of putting to an end a great deal of useless, expensive, and misapplied therapeutic efforts.

Further Suggestions

But let us continue. Do constipated people really need aperients, or would they after a time develop a normal habit if given a placebo medicine? Is there any association between constipation and halitosis? Is emphysema a hereditary disease, or can it perhaps be divided into a group that is hereditary and another that has a known aetiology such as asthma or bronchiectasis? And, finally, does tooth-brushing prevent caries?

This is where we came in. These are only a few suggestions about problems which might be investigated in general practice; most of them, I submit, have both interest and practical importance. There must be hundreds of other problems, the best ones being those that one thinks out for oneself. Some of them come to mind by reflecting on one's experience; for instance, by getting a clinical impression that a certain complaint seems to be particularly common in workers at a certain trade, and collecting statistical information to find out if the impression is correct. Others will come as heaven-sent opportunities; for instance, you might discover by careful observation something about the epidemiology of Bornholm disease, or even poliomyelitis, or you might find a combination of two rare dominant genes, such as those of retinitis pigmentosa and von Recklinghausen's disease, occurring in one and the same family. Quite a small group of carefully compiled observations on the behaviour of these genes in three generations would suffice to show whether they were carried on the same chromosome pair (see Fraser Roberts, 1945), and thus assist in the mapping of the human chromosomes.

Conclusion

I have not consulted any literature on the suggestions I have made. The answers to some of the questions may be already known, but I doubt if they are. Any investigation of these problems would have to be carefully thought out and a plan of campaign prepared. Literature might have to be consulted. Snags would be inevitable, and changes of plan would be required. Very few researches work out as one expects. Above all, one must be prepared for the results to be negative or to be the reverse of what one would like to prove. A willingness to admit defeat is part of the attitude of mind, and, as I said at the beginning, it is really only the attitude of mind which distinguishes the research worker from his fellows.

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IS EARLY TREATMENT ESSENTIAL IN CANCER?

BY

SIDNEY RUSS, C.B.E., D.Sc.

In view of the many characteristics of cancer, the advice often given, that treatment should begin as soon as possible after symptoms are recognized, is almost taken for granted; but this point of view has recently been challenged in the *British Medical Journal* (1952). Over and over again in the valuable *Survey of Cancer in London* by W. L. Harnett (1952) we meet a concluding statement such as: "There is no significant difference between the survival rates of those who come under treatment within the first six months of noticing symptoms and those in whose cases the delay was longer." The treatment in question has for the most part been surgical or radiological. The author was careful to point out that this does not mean that there is no difference in the survival rates of patients when treated in the *early* or *late stages* of the disease. It is because there are often such significant differences that the urge for early treatment arises, but it does not follow that the duration of symptoms before treatment is necessarily brief in Stage I cases or long in the later stages.

Details of 695 Cases

I have been fortunate in gaining access to data relating to the radiation treatment of cancer of the cervix uteri in 695 cases the details of which were not given in the survey mentioned. In Table I the data show how the duration of symptoms before treatment is distributed for Stages I–IV of the disease.

TABLE I

Duration of Symptoms Before Treatment	Stage I	Stage II	Stage III	Stage IV
1–3 months ..	74	128	88	27
3–6 ,, ..	26	61	46	14
6–12 ,, ..	22	45	31	6
Over 12 ,, ..	13	31	26	11
Not known ..	14	22	9	1
Totals ..	149	287	200	59

Further data in Table II respecting these patients show how the numbers of five-year survivals are related both to the stage of the disease and to the duration of symptoms before treatment.

The whole of the subsequent argument here is based upon the validity of the data under the heading "Duration of symptoms before treatment"; this is a quantity which depends in no way upon medical observation, because it is what the patient thinks at the time the questions are put.

TABLE II

Duration of Symptoms Before Treatment	Stage I		Stage II		Stage III		Stage IV	
	Alive	Dead	Alive	Dead	Alive	Dead	Alive	Dead
1–3 months ..	32	42	46	82	19	69	2	25
3–6 ,, ..	14	12	15	46	5	41	—	14
6–12 ,, ..	12	10	14	31	5	26	1	5
Over 12 ,, ..	8	5	8	23	1	25	1	10
Not known ..	6	8	5	17	—	9	—	1
Totals ..	72	77	88	199	30	170	4	55
5-year survivals	48·3%		30·5%		15%		7%	

No one would claim that it is trustworthy in every detail, but there is probably a rough truth about the complete record, and this is borne out by comparing it with the results of two other inquiries into cancer treatment and its results. The General Register Office published in 1950 *Cancer Registration in England and Wales*, by Dr. Percy Stocks. The section devoted to cancer of the cervix uteri refers to 3,759 patients, and there is a general similarity in the distribution of the duration of symptoms before treatment, when compared with that in question here (see Table III).

Further, we have data upon 700 patients with cancer of the cervix uteri from the Marie Curie Hospital records.

TABLE III

Duration of Symptoms Before Treatment	Source of Data		
	Survey of Cancer in London	England and Wales General Register Office	Marie Curie Hospital
0–6 months ..	464	2,726	476
6–12 ,, ..	104	443	187
12 months and over	81	378	107
Not stated ..	46	212	—
Totals ..	695	3,759	770

The data in Table II show that patients in Stage I have about three times the five-year survival rate of those in Stage III, yet the duration of symptoms at the time of the first treatment is not related in any simple manner with these survival rates; in fact, in Stage I cases there are slightly more dead than alive when this duration is 1–3 months, but there are slightly more alive than dead when the duration is 6–12 months or over.

Gilmour, Glucksmann, and Spear (1949) conclude that "there does not appear to be any correlation between duration of symptoms and radiocurability of tumours." The authors remark that "this finding is surprising," but refrain from commenting upon its implications other than saying that "the clinical extent of the disease depends both on the rate of growth of the tumour and on the length of time for which it has been present." It will be agreed that in Stage III cases which have a duration of symptoms of 1–3 months the tumours have grown more rapidly than in Stage I cases having a duration of over twelve months. It is suggested that one of the reasons why these Stage I cases do well under radiation treatment is that the malignant cells are in a state of slow growth, and as such are more susceptible to irradiation than the rapidly growing ones. In support of this suggestion some experimental studies upon tumour growth by Miss G. M. Scott and myself (1933, 1940) may be recalled. In these papers and in the laboratory records there is abundant evidence to show that the dose of *x* rays required to produce a lethal effect has to be increased when the tumours are growing rapidly. This is in no way contrary to clinical experience that with tumours of differing histological types rapidly growing ones are often found to be more susceptible to radiation than others which grow slowly. For one and the same histological type it is suggested that the more rapidly growing tumours will need more *x* rays than the slow ones in order to achieve a lethal action. The results suggest that in the radiation treatment of Stage I cases of short symptom duration the dose be increased.

If we suppose that the foregoing statistical data are indeed factual, they certainly run counter to some of the currently held views about early and late cancer, and so they are matters for comment. In the first place it is to be noted that an appreciable percentage of Stage I cases exhibit a duration of symptoms before treatment of about 12 months; *they do not over this period become Stage II or III cases.* To account for this we may postulate a resistance on the part of the patient, and the most likely expression of this would be in the stroma reaction amid the tumour tissue; further, the results of radiation treatment in Stage I cases with a duration of symptoms 6–12 months are just as favourable as in those patients having a duration of symptoms of a few months. Modern views about radiation treatment are inclined to attribute good results not only to the damaging effects of radiation upon cancer cells but to a supporting response from the connective-tissue stroma; this is the underlying philosophy of Dr. B. Jolles, who maintains that cancer radiation treatment is largely a connective-tissue problem. In Stage I cases with a duration period of 12 months or more two of their outstanding features would appear to be clarified by thinking on these lines.

To turn to the initial considerations, the question inevitably and cogently arises whether the plea for early treatment has a warrant behind it. If Stage I patients respond to radiation treatment just as well whether they are treated one or twelve months after the appearance of symptoms it looks as though urgency is not of the first importance. But this line of thought is too restrictive; all Stage II, III, and IV cases of cervical cancer will at one time have been Stage I cases,* though not declared, and as such could have been more easily and more successfully treated; this is the outstanding fact about which all statistics do agree.

If we want to be absolutely precise in this matter, the warning should be that patients are advised to seek medical advice as soon as possible when certain symptoms appear, so that if treatment is necessary they should be in an early stage of the disease when treatment is carried out.

These symptoms have appeared in thousands of women who have had no idea of their significance. If some of the leading facts were properly presented and taken to heart by a big fraction of the population, it is a fair inference that the death rate from cancer of the cervix uteri would be reduced.

I am indebted to the British Empire Cancer Campaign for access to data, and to Colonel Harnett for their elucidation.

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*The question of multicentric origin need hardly be considered in cervical cancer.

The Ministry of Education has recently brought out a revised edition of List 42, a complete list of special schools and training establishments in England and Wales for the physically or mentally handicapped. Schools for blind, deaf, epileptic, or mentally retarded children are listed, together with details of the age range and the area from which pupils are mainly drawn. Hospital schools and training institutions for disabled people are also included in this list, which is obtainable (price 2s.) from Her Majesty's Stationery Office, York House, Kingsway, London, W.C.2.

EARLY DIAGNOSIS AND TREATMENT OF CARCINOMA OF THE NOSE

BY

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It is obvious that for the successful treatment of carcinoma of the nose early diagnosis is essential. The following observations are confined to carcinoma and sarcoma; all other growths are excluded. Early diagnosis is always difficult and sometimes impossible, because carcinoma in itself does not produce any specific symptoms or signs; it is only when the cancer cells form a tumour that a series of mechanical results appear. Furthermore, the development of these is slow and insidious, particularly in a hidden cavity like the nose or anterior fossa of the skull. The patient does not consult a doctor until such symptoms have become well marked or intolerable. General signs, such as blood changes, are of no practical value in the early diagnosis.

A brief review of the pathological anatomy is necessary. Malignant growths of the nose have been divided into extranasal and intranasal (Woodhouse Price, 1935). The extranasal growths, which involve the nasal cavities secondarily, consist of two groups, the upper and the lower.

Extranasal Carcinomata

The upper group consists of those growths which arise in the anterior fossa of the skull, the sphenoid, or nasopharynx. For example, the meningioma of the olfactory groove bursts through the cribriform plate and roof of the lateral mass of the ethmoid and presents as a vascular polypoid tumour high up in the olfactory cleft of the nose. This tumour has been mistaken for a simple polypus, but a biopsy from the deep tissues should be made when such a vascular and suspicious polypus appears. The first and most frequent sign is a continuous and severe frontal headache. Loss of the sense of smell should be an early sign, but patients rarely complain of the loss of smell, particularly if they are smokers. The loss of smell is thought to be trivial by most men and is often ignored. When the growths involve the orbit paralysis of an ocular muscle and displacement of the eyeball occur. Loss of sight and optic atrophy follow the anosmia. A meningioma involving the nose is rare, and I have seen only four cases. Harvey Cushing (1927) has reported a series of cases in detail. These meningiomas present a syndrome—loss of smell, optic atrophy, and altered personality. Sometimes the patient is seen for nasal obstruction or frontal sinus headache. A meningioma may not be a carcinoma, but from a clinical point of view it behaves like one, and all four patients who were seen by me died within 12 months from the day I first saw them.

The growths which arise in the sphenoid seem to begin in the great wing of the sphenoid near the foramen ovale. They spread to the sphenoidal sinus or creep along the base of the skull and appear in the posterior and upper part of the nose or in the nasopharynx. The enlarged secondary lymphatic nodes along the posterior border of the upper third of the sternomastoid muscle first attract the attention of the patient or doctor, or there is a blood-stained nasal discharge and paralysis of an ocular muscle first on one side and then on both, and complete ophthalmoplegia may follow. These cases are often first seen in the ophthalmic or neurological department; then they are sent to the oto-laryngologist for an investigation of the nose as a possible cause of the loss of sight (retrobulbar neuritis) or of the displacement of the eyeball and the headache.

The lower extranasal group of carcinomata are those which begin in the maxillary alveolus, the cheek sulcus, or the palate. I have the notes of 18 of these cases. The growth quickly burrows into the floor of the antrum and spreads upwards. It occupies the antrum by its extension, and I have not seen a primary carcinoma of the mucosa of the antrum. The lower group of cases go to the dental surgeon for pain or a loose tooth. If the tooth is extracted the socket does not heal and may sprout granulation-like tissues, or, more commonly, a sinus arises, discharging foul pus which the patient can smell and taste. When the sinus is explored a soft necrotic vascular growth is discovered occupying the alveolus and the floor of the antrum. A swelling or deformity in this area may be the first sign. Later a typical epitheliomatous ulcer develops. These cases can be diagnosed much earlier because they are seen and felt more easily and pain is an early symptom. Often a patient does not see a doctor or dental surgeon until a tumour or deformity is present. An epithelioma of the skin of the nose or a rodent ulcer involving the nasal cavity has been seen occasionally.

Intranasal Carcinomata

Intranasal carcinomata arise in the lateral mass of the ethmoid and the middle meatus of the nose at a point where the upper edge of the middle turbinate blends with the middle ethmoid cells (Fig. 1). The growth quickly invades the orbit through the anterior ethmoid cells to form a large nodule of growth between the orbital periosteum and its bony floor. It surrounds the infraorbital nerve, and this at first suggests that the growth may have begun in that area. When this occurs the eyeball is displaced upwards, but is not invaded by the growth. At about the same time the growth, taking the path of least resistance, extends into the antrum and expands its walls, but does not invade the mucosa. Then it bursts through the facial wall near the inferior orbital foramen, where it soon involves the cheek. The growth spreads upwards in the ethmoid to the roof and floor of the anterior fossa and into the sphenoidal sinus, but it is not often that the frontal sinus is invaded. Owing

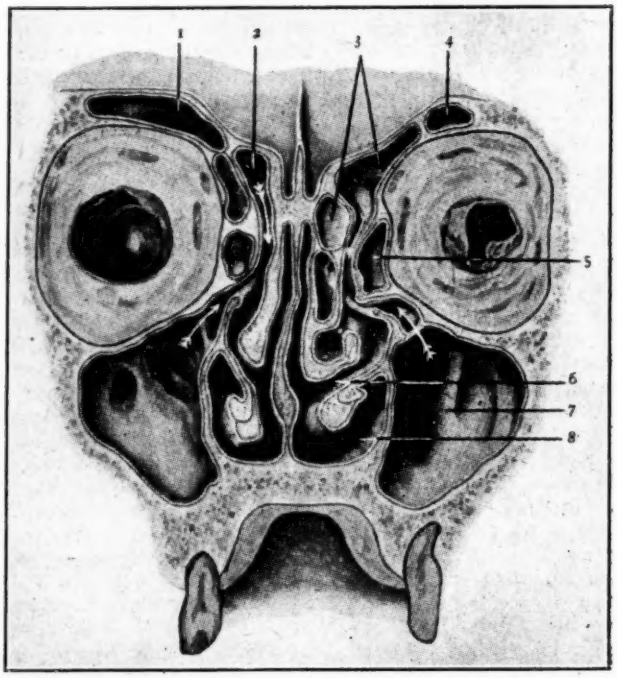

FIG. 1.—The nasal and paranasal air cavities (coronal section) on the plane of the maxillary ostia (viewed from behind). 1, Left frontal air cavity. 2, Left anterior ethmoidal air cells. 3, Right anterior ethmoidal air cells. 4, Right frontal air cavity. 5, Right ethmoidal bulla. 6, Right middle meatus. 7, Right maxillary air cavity. 8, Right inferior meatus. (Reproduced from A. L. Turner and F. E. Reynolds's *Intracranial Pyogenic Diseases*, by permission of Messrs. Oliver and Boyd.)

to the confined space of the nose and the pressure of its walls the growth becomes inflamed and necrotic and its surface sloughs.

Fig. 2 is a photograph of Specimen No. 49 in the Museum of the Ferens Institute, Middlesex Hospital. It is a carcinoma of the right ethmoid which has involved both orbits and antra. The primary growth appears to have originated in the right middle ethmoidal cells and then extended through the lateral mass of the ethmoid into the orbit. The growth has crept between the bony floor of the orbit and the thick orbital periosteum, then filled the inner half of the orbit, displacing the eyeball outwards and upwards. At the same time the growth has filled the nasal cavity as far as the upper edge of the inferior turbinated bone. A prolongation of the growth, taking the line of least resistance, has penetrated the middle meatus of the nose to fill the antrum

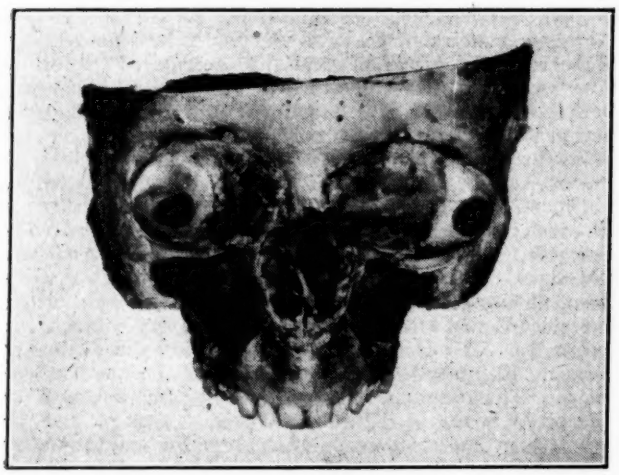

FIG. 2.—Photograph of a carcinoma of the right ethmoid, involving both orbits and antra.

with a rounded fleshy tumour. This prolongation has eroded the thin facial wall of the antrum near the infra-orbital foramen and is beginning to invade the cheek, but not the mucosa of the antrum. It has bulged through the thin posterior wall of the antrum into the spheno-maxillary fossa, pushing the mucoperiosteum of the antrum with it and bulging into the pterygo-maxillary fossa. The facial walls of both antra have been removed to show the growth. In an upward direction the growth has eroded the roofs of both orbits and invaded the anterior fossa of the skull.

It is difficult to trace the path of the growth from the right ethmoid to the left nasal cavity and orbit, but in this case the growth has crept along the cribriform plate of the ethmoid and has expanded the bridge of the nose and filled the left nasal cavity. The growth in the left nasal cavity has extended into the orbit, the antrum, and the spheno-maxillary fossa in the same way as that in the right nasal cavity. The displacement of both eyeballs outwards and upwards and the expansion of the bridge of the nose produced an appearance known as "frog face." The growth has protruded through the upper part of both posterior nares into the nasopharynx. The section for microscopy showed a squamous carcinoma of the undifferentiated type. It is interesting to note that both frontal lobes of the brain were densely adherent to the dura mater and falx of the anterior fossa of the skull. There was a large subdural haemorrhage on the right side, and the growth had perforated the dura on the left. The patient probably died from a subdural haemorrhage and meningitis.

An epithelioma of the anterior and lower part of the nasal septum is not so common as would be expected; I have seen only two cases. It takes the form of an epitheliomatous ulcer, and is not the cauliflower-like growth which arises from the ethmoid and quickly fills the nasal cavity. It infiltrates rapidly and is more extensive than it appears to be on examination.

Signs and Symptoms

A perusal of the notes of 60 cases of ethmoidal carcinoma indicated that the first symptoms were pain in the cheek and around the eye, with a blood-stained offensive discharge. The odour is often characteristic. Sometimes epistaxis from the upper part of the nose occurred. Lacrimation with injection of the conjunctiva of one eye is an early symptom (C. P. Robinson, 1934, personal communication). Obstruction of the naso-lacrimal duct is a late sign and is rare. Oedema of the middle meatus of the nose, which bleeds easily when touched, is suspicious. Stereoscopic *x*-ray photographs of the ethmoids and antra are essential, but a negative *x*-ray picture is inconclusive and should be ignored. Photographs taken three or six months after complete excision may show an early recurrence.

These symptoms and signs in a patient of cancer age should suggest the presence of a growth, and if there is any doubt a thorough exploratory operation, with preparations for complete excision, should be performed to obtain a clear view of the interior of the nose by expanding the nostrils with a Killian nasal speculum. If necessary the antrum is inspected through an opening made in the canine fossa. Occasionally a patient of cancer age visits the department complaining of nasal obstruction, and polypi of recent onset are seen. When some of the polypi are removed the free bleeding and deeper swelling suggest carcinoma. Much too frequently these cancer patients are not seen until the above symptoms and signs have been present off and on for six to eight weeks. Then the patient appears with proptosis and an upward displacement of the eyeball, or there is oedema of the lower eyelid at the inner canthus and slight swelling of the cheek. Unilateral nasal obstruction occurs late and it is not often an early complaint. At this stage the vascular granuloma-like growth can be seen in the middle meatus and a blood-stained purulent discharge of characteristic odour is present. *X*-ray photographs show a marked opacity of the ethmoid and antrum.

Microscopy of the growth does not really hasten the diagnosis. A negative biopsy is valueless and should be ignored. Frequently a polypoid growth is reported to be inflammatory or granulation tissue. This report is common in cases of lymphosarcoma. The surface of a nasal carcinoma is necrotic and the histological appearance of the growth is altered. Similarly, deep *x*-ray therapy and radiotherapy produce inflammatory changes and fibrosis. A biopsy is taken from tissue as deep as possible in the suspected growth. I have examined 23 microscopical sections of ethmoidal carcinoma without finding any evidence to show where the growth started. In a few cases in which the nasal mucosa is present it is free from growth. In the others the mucosa is absent or has been destroyed by sloughing or by the growth. The cancer cells spread in the submucous tissues rapidly and erode the thin bone. It is sufficient to say that the types of carcinoma of the nose are similar to those of the lung, where three types are reported: squamous carcinoma is the commonest; adenocarcinoma is not often seen; and undifferentiated carcinoma is frequent. The type of nasal carcinoma is not usually so clearly defined. There is considerable variation in the microscopy of nasal carcinoma, and many different types have been described. In 1933 Ohngren recorded that the incidence of carcinoma of the nose was 1 to 2% of all deaths from cancer. Up to 1950 the classification of cancer of the nose in the Registrar-General's returns was unsatisfactory. The cases were grouped under (*a*) cancer of accessory sinus, frontal or maxillary, and (*b*) cancer of the nasal cavity. The figures available show that the incidence of cancer of the nose has not increased like that of the lung (A. Bradford Hill, 1952, personal communication). The incidence of cancer of the lung in 1920 was 1.5% of all cancer deaths. In 1947 it was 19.7%.

There were only six cases of lymphosarcoma among the 60 cases; one was associated with severe lymphatic leukaemia and may be called a leukosarcoma. Lympho-

sarcoma is a very vascular rapidly growing polypoid growth, and the first sign is diplopia with proptosis and enlargement of the upper cervical lymphatic nodes. Recurrence after radiotherapy and excision occurs within six months. At the biopsy the growth has been mistakenly labelled inflammatory. Secondary growths are decidedly early. All the six patients with lymphosarcoma died within six months in spite of treatment. Lymphosarcoma is said to be more sensitive to radiotherapy than the epitheliomata. The histology of the carcinomata may indicate which growths are sensitive to radiotherapy.

Aetiology and Differential Diagnosis

The aetiology is not very helpful. Any of the symptoms mentioned above in a patient of cancer age is an indication of a growth. Males and females are both affected, males a little more frequently. The occupations of the patients are very varied, but prolonged and constant exposure for some years to irritating dust has been a contributory cause in the past. Recently, improved and better ventilation and suction dust-extractors have more or less eliminated this cause. The fact that the direct or contributory causes of carcinoma of the nose are unknown makes prevention difficult, except in the elimination of an irritating dust.

The differential diagnosis is not difficult. Syphilis and tuberculosis have resembled carcinoma. Neglected tertiary syphilis with necrosis of bone and gummatous infiltration of long duration is not often seen to-day. If there is any doubt, a Wassermann test is done, but it should not be allowed to delay treatment. Tuberculosis of the nose takes the form of lupus, and one or two cases of epithelioma stated to have followed a very chronic and much-treated lupus have been reported. Epithelial papillomata of the nose arising from the nasal epithelium are decidedly rare. I have seen only four cases during a period of 30 years. Papillomata are multiple and, if not removed completely, recur rapidly. Sections of a small piece of the papilloma for microscopy can be mistaken for carcinoma.

Treatment

The results of radium and deep *x*-ray therapy have been disappointing. Success has been achieved in a small number of early cases, but it is doubtful whether the inoperable advanced cases derive enough benefit to make that method worth while. The hope of success and the satisfaction that an effort is being made to relieve the patient are counterbalanced by the misery and the discomfort of an *x*-ray burn and by economic considerations. Some growths have been known to flare after radiotherapy, although the radiosensitive lymphosarcoma may disappear with the treatment, but secondary growths soon appear. Unfortunately, there is no satisfactory alternative treatment for the inoperable advanced case, and adequate doses of morphine sulphate have to be given by mouth. A careful selection of cases and the interruption of treatment if no improvement is established would relieve the overloaded radiotherapeutic departments. It is possible that the site of origin of the growth is not exposed sufficiently to allow good access to the growth. Deep *x*-ray therapy given after an operation for the removal of the growth and hard palate, to expose the area involved, seems to produce better results. *X*-ray therapy and teleradium have been tried before operation, but the postponement of the operation, the lowered state of nutrition, and the risk of increased sepsis counteract any beneficial result. *X*-ray burns and general disturbances occur more often after a second course of treatment. The combination of electro-surgery and *x*-ray therapy, with free access to the growth to facilitate complete excision by radical surgery as early as possible, is now advocated.

The operations carried out have had these two principles: first, a thorough exposure of the neoplasm to define its limits, and, secondly, complete excision by diathermy, with a margin of normal tissue where possible. The orthodox anatomical operation of excision of the upper jaw has been discarded. The teeth are put in order as soon as possible after the patient is first seen, and, because half of the palate is to be removed, a denture or obturator of soft vellum rubber or of acrylic resin is made and inserted immediately after the completion of the operation. The most satisfactory form of anaesthesia is the intratracheal, and it has been employed without any disadvantage. The external carotid artery was ligated on two occasions only, because it was considered that ligation did not diminish the haemorrhage. On the other hand, Ohngren has proved to his satisfaction that secondary haemorrhage after diathermy was materially diminished by ligation of the external carotid. He also advises that the ligature should be applied above the superior thyroid artery, because the clot has been known to be detached and carried into the internal carotid artery. Ligation is of more value when diathermy is applied to the fauces and soft palate.

In the ethmoidal or intranasal group of cases permission should be obtained to enucleate the eyeball if a more thorough clearance of the orbit is likely to be required, but the orbital periosteum protects the contents of the orbit. I have not seen a case in which the orbital periosteum has been penetrated or the orbital fat infiltrated. The growth occupies the orbit. Good access to the orbit is obtained by removing the lateral mass of the ethmoid and the floor of the orbit without removal of the eyeball. The eyeball is not involved by the growth, and when it has been necessary to enucleate it the case, in my experience, is hopelessly inoperable. The loss of an eye is demoralizing, and it does not arrest the progress of the growth. The modified Ferguson incision is made from the fronto-nasal suture down the side of the nose, around the nostril, and through the upper lip. This incision can be made with the diathermy needle, which has the advantage of diminishing the haemorrhage. The cheek is reflected upwards and outwards to the malar bone, the infraorbital margin is defined, and the whole bony wall of the side of the nose and antrum as far outwards as possible is removed. The ethmoid is exposed by removing the whole of the nasal bone and the ascending process of the maxilla right up to the fronto-nasal suture. The tumour, with the floor of the orbit, is peeled off the orbital periosteum. The ethmoid, infiltrated by the growth, is coagulated by the diathermy button and removed up to the base of the skull and as far back as the sphenoid.

Diathermy arrests the haemorrhage, and is applied whenever practicable, and to any areas where the growth is suspected. The hard palate and floor of the nose are not infiltrated by the tumour, but they should be removed to form a window, so that the area of the growth can be inspected and diathermy and radiotherapy applied after the skin incision has been closed. The technical details of the operation have evolved, and have been improved in the later cases, as more experience has been gained. All the patients made an uneventful recovery, and not one died from the immediate or remote effects of the operation. Meningitis and injury to the eyeball were expected, but particular care was taken in dealing with the tumour in these areas. The contents of the orbit can be protected by a thin spatula insulated by a covering of rubber or vulcanite. Ohngen, who has operated on a large number of these cases with diathermy, has seen meningitis, cerebral oedema, and cerebral abscess occur with and without radium application. The application of diathermy to the orbital periosteum, and also radium exposure, have been followed by necrosis of the eyeball. In three of the above cases blindness from optic atrophy ensued with the recurrence of the growth. After diathermy, patients often complain of the offensive odour in spite of irrigation with eusol. Ohngren has painted the charred area with a 2% permanganate solution and irrigated it with a 1 in 2,000 permanganate solution with success. Penicillin reduces the sepsis.

The lower extranasal group of carcinomata of the alveolus were attacked by dividing the upper lip in the midline and carrying the incision into the nostril, the cheek then being reflected upwards so as to expose the alveolus thoroughly. Division of the upper lip is not a necessity, and sufficient

retraction of the cheek and upper lip can be obtained by a long incision in the cheek sulcus from the malar ridge to a point across the midline of the incisor teeth or alveolus. The antrum is opened high up on the facial surface of the maxilla to expose the upper limit of the growth. The neoplasm is then excised, with a free margin of healthy tissue. The floor of the antrum and a large area of the hard palate are removed, the cheek is carefully examined, and any growth is widely excised by diathermy. The whole of the facial wall of the antrum is removed, then the square block of the alveolus and palate to be excised is marked out by cutting through the muco-periosteum with the diathermy needle. The diathermy incision is made transversely across the alveolus and palate to the midline behind the growth. A similar transverse incision is made in front of the growth, and the two incisions are joined by a cut along the midline of the palate.

The block of bone is removed by first dividing the bone with slightly angular bone forceps in front, then dividing the ascending nasal process transversely at the level of the attachment of the inferior turbinate, across the alveolus, and along the midline to the posterior cut. The posterior transverse incision through the bone is completed last, because haemorrhage from the descending palatine vessels is more severe and because it is more easily controlled when the block of bone has been removed. The window in the palate is closed by a permanent dental obturator made when the wound has healed. The fixation of the obturator is facilitated and the comfort of the patient increased if as much of the heel or tuberosity of the maxilla and of the alveolus of the incisor region is left, consistent, of course, with a complete removal of the growth.

Encouraging Results

At the operation it is often discovered that the tumour is deeper and more extensive than anticipated; on the other hand, cases which seem to be hopeless often do better than expected. The difficulty of early diagnosis and the inaccessibility of ethmoidal carcinoma make complete excision somewhat uncertain; nevertheless we are encouraged by the increasing number of successful cases in recent years. Out of 52 cases of all types of carcinoma Capps (1950) has reported 14 free from disease for five years or more. Three patients with lymphosarcoma all died.

Ohngren records 38 cases of carcinoma out of 104 free from recurrence after two years.

Windeyer and Wilson (1950) had 69 cases between 1925 and 1935; of 97% who were traced 18.8% survived the five-year period. Up to 1943 the percentage of three-year survivals was increasing in spite of the fact that all cases, however advanced, were being treated. The eight cases of sarcoma treated before 1937 did not survive the five-year period. However, operation relieves the patient, and he has the satisfaction of knowing that a determined effort has been made to rid him of the disease with some hope of success. The condition of the inoperable patient is truly a miserable one.

Summary

A brief review of the pathological anatomy of nasal carcinoma is given.

Carcinomata of the nose are divided into two groups—the extranasal and the intranasal.

The extranasal group consists of those growths which rise from areas outside the nose and later involve the nasal cavity. Carcinoma of the alveolus of the maxilla spreads upwards to invade the antrum. Carcinoma of the sphenoid, nasopharynx, and anterior fossa of the skull spreads downwards to the nasal cavity.

The intranasal group consists of growths which arise within the nasal cavity, such as the ethmoidal carcinoma.

The origin and spread of an ethmoid carcinoma is illustrated.

The early symptoms, signs, and diagnosis of these growths are described.

The treatment preferred is radical electrosurgery, and the principles of the operation are given.

I am indebted to Mr. C. P. Wilson and the Ferens Institute of the Middlesex Hospital for the opportunity of seeing a number of cases and specimens; also to Professor R. W. Scarff and Dr. A. C. Thackray, of the Bland-Sutton Institute, who reported on some of the microscope slides.

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A SURVEY OF 647 CASES OF LEUKAEMIA, 1938-51

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In view of the extensive literature on the subject of leukaemia, it is surprising how few reports have dealt with the relative incidence and comparative features of the different types of this disease in recent years. Standard works on haematology in Great Britain—for example, Whitby and Britton (1950)—still quote the survey of the London Hospital records of 1912 to 1927 (Panton and Valentine, 1929) for information on these points. Over the past few years an impression has been forming that in Scotland there has been both an increase in the occurrence of leukaemia and a deviation from the generally accepted incidence of the different varieties. The present report describes an investigation designed to supply information on these points.

Independent surveys have been carried out in two centres, Edinburgh and Aberdeen, of the cases of leukaemia appearing in hospitals over the fourteen-year period 1938 to 1951. The Edinburgh series (E) comprises cases seen in the Edinburgh Royal Infirmary, the Royal Hospital for Sick Children, and the other main hospitals in the Edinburgh area. A large number of these cases have been dealt with by the Regional Centre for Radiotherapy, situated at the Royal Infirmary. The Aberdeen series (A) includes cases seen in the Aberdeen Royal Infirmary, the Woodend General Hospital, and the Royal Hospital for Sick Children, Aberdeen.

It is believed that the combined series includes a very large proportion of the total number of cases of leukaemia occurring in the eastern half of Scotland during the fourteen years under review. Only those cases which were subjected to expert haematological study have been included in the series from both centres, and in a great many instances the data presented were provided by the investigational and diagnostic services of the University

Departments of Medicine in Edinburgh and Aberdeen. Bone-marrow studies have been included in the examination of a large proportion of the cases quoted.

The total number of cases of leukaemia in the combined series was 647, consisting of 440 cases in series E and 207 in series A.

Type Incidence

Cases have been classified, in the generally accepted manner, as lymphatic, myeloid, or monocytic, with further subdivision into acute or chronic forms in the lymphatic and myeloid varieties. No cases of chronic monocytic leukaemia have been encountered.

Table I shows the incidence of the different types in order of frequency for the two separate surveys and for the combined series. Chronic lymphatic leukaemia was clearly the

TABLE I.—*Incidence of Types of Leukaemia*

Type of Leukaemia		Series E	Series A	Combined Series
Chronic lymphatic	No. of cases	132 (30·0%)	75 (36·2%)	207 (31·9%)
	,, aleukaemic	18 (13·6%)	19 (25·3%)	37 (17·9%)
Chronic myeloid	,, of cases	122 (27·7%)	47 (22·7%)	169 (26·1%)
	,, aleukaemic	5 (4·1%)	4 (8·5%)	9 (5·3%)
Acute lymphatic	,, of cases	107 (24·3%)	37 (17·9%)	144 (22·3%)
	,, aleukaemic	31 (28·9%)	24 (64·9%)	55 (38·2%)
Acute myeloid	,, of cases	46 (10·5%)	24 (11·6%)	70 (10·8%)
	,, aleukaemic	12 (26·1%)	10 (41·7%)	22 (31·4%)
Monocytic	,, of cases	33 (7·5%)	24 (11·6%)	57 (8·8%)
	,, aleukaemic	9 (27·3%)	8 (33·3%)	17 (29·8%)
Total No. of cases of all types		440	207	647
,, ,, ,, aleukaemic cases		75 (17·0%)	65 (31·4%)	140 (21·6%)

Note: In each series the number of cases of each type of leukaemia is expressed as a percentage of the total cases of all types in that series, whereas the number of aleukaemic cases is expressed in each instance as a percentage of the number of cases of that particular type.

commonest, accounting for 207 (31.9%) of the total cases; chronic myeloid leukaemia was next in frequency with 169 cases (26.1%); then acute lymphatic leukaemia with 144 cases (22.3%), acute myeloid leukaemia with 70 cases (10.8%), and monocytic leukaemia with 57 cases (8.8%). It should be noted that the same order was found in both surveys.

The incidence of the aleukaemic form of the disease is also shown in Table I. Aleukaemia was defined simply as being present when the total peripheral white-cell count did not exceed 10,000 per c.mm. In the combined series, 140 of the 647 cases were aleukaemic (21.6%). Acute lymphatic leukaemia had the highest proportion of aleukaemia—55 out of a total of 144 cases (38.2%), and the lowest incidence was found in the chronic myeloid variety (5.3%). In acute myeloid and monocytic leukaemia 31.4% and 29.8% respectively were aleukaemic, and in the chronic lymphatic group 17.9% were aleukaemic. In the individual series the incidence of aleukaemia showed the same type variation, though there was throughout a higher incidence of aleukaemic forms in series A than in series E.

Age Incidence

The age incidence of chronic lymphatic leukaemia in the combined series of 207 cases is shown in Fig. 1. The range was from 23 to 84 years of age, while the average was 61.5 years. Series E and A agreed closely, the average ages being 60.3 and 62.5 respectively. The age distribution in the combined total of 169 cases of chronic myeloid leukaemia is shown in Fig. 2. Here the range was from 7 to 80 years of age, while the average was 49.8 years. (The average in series E was 50.1 and in series A 49.1 years.) Fig. 3 shows that the 144 cases of acute lymphatic leukaemia had an average age incidence of 20.4 years, with a range from 2 months to 81 years. (The two surveys gave averages of 19.4 and 23.6 respectively.) The histogram of the 70 cases of acute myeloid leukaemia is shown in Fig. 4. Ages ranged from 14 months to 80 years, and the combined

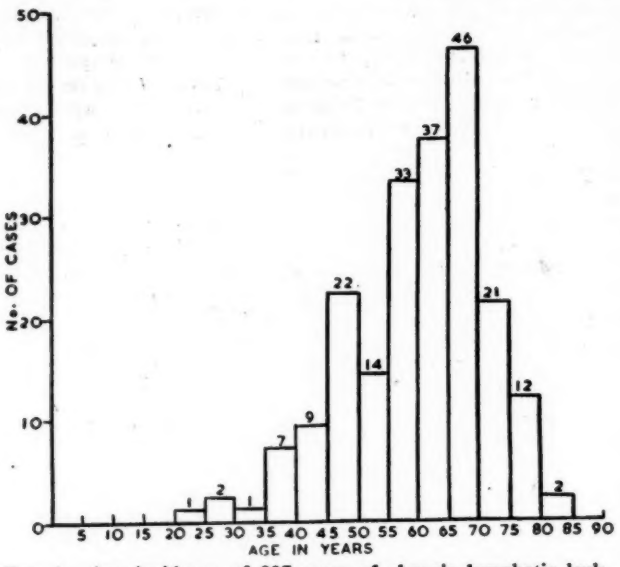

FIG. 1.—Age incidence of 207 cases of chronic lymphatic leukaemia. Range, 23–84 years; average, 61.5 years. Series E, 60.3 years. Series A, 62.5 years.

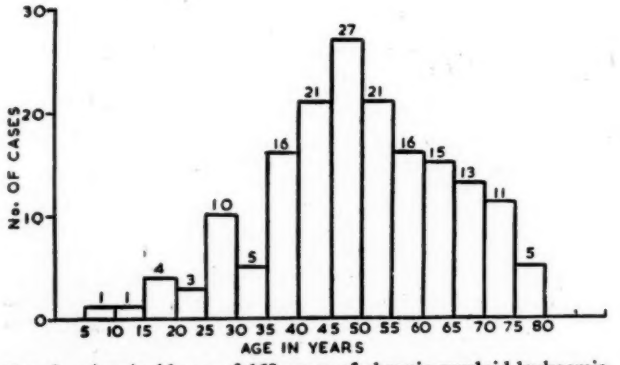

FIG. 2.—Age incidence of 169 cases of chronic myeloid leukaemia. Range, 7–80 years; average, 49.8 years. Series E, 50.1 years. Series A, 49.1 years.

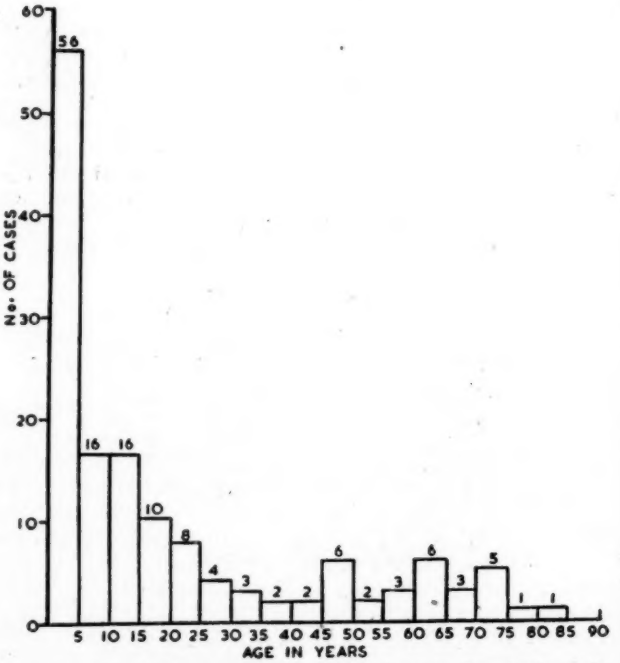

FIG. 3.—Age incidence of 144 cases of acute lymphatic leukaemia. Range, 2 months to 81 years; average, 20.4 years. Series E, 19.4 years. Series A, 23.6 years.

average was 38.9 years. (The separate averages were 37.0 and 42.6 years.) Monocytic leukaemia (57 cases) is similarly illustrated in Fig. 5. The range of ages was from 9 months to 86 years, with an average of 40.0 years (series E 38.8 and series A 41.8 years).

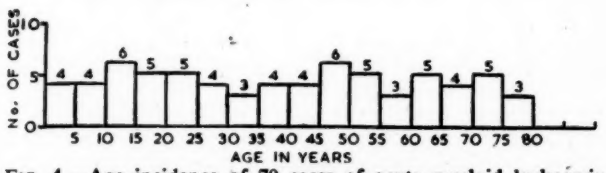

FIG. 4.—Age incidence of 70 cases of acute myeloid leukaemia. Range, 14 months to 80 years; average, 38.9 years. Series E, 37.0 years. Series A, 42.6 years.

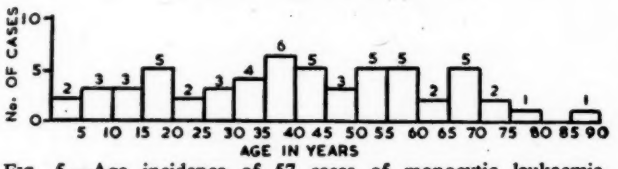

FIG. 5.—Age incidence of 57 cases of monocytic leukaemia. Range, 9 months to 86 years; average, 40.0 years. Series E, 38.8 years. Series A, 41.8 years.

Sex Incidence

The sex incidence in the two surveys and in the combined series is shown in Table II. The aleukaemic cases are also shown. The overall incidence was approximately 7 males

TABLE II.—*Sex Incidence*

Type of Leukaemia		Sex	Series E	Series A	Combined Series	Totals	
Acute	Lymphatic	M	58 (16)	20 (11)	78 (27)	M 142 (46)	M 352 (67)
		F	49 (15)	17 (13)	66 (28)		
	Myeloid	M	22 (5)	12 (5)	34 (10)	F 129 (48)	
		F	24 (7)	12 (5)	36 (12)		
	Monocytic	M	19 (6)	11 (3)	30 (9)		
		F	14 (3)	13 (5)	27 (8)		
Chronic	Lymphatic	M	84 (10)	46 (10)	130 (20)	M 210 (21)	F 295 (73)
		F	48 (8)	29 (9)	77 (17)		
	Myeloid	M	61 (1)	19 (0)	80 (1)	F 166 (25)	
		F	61 (4)	28 (4)	89 (8)		

The figures in parentheses indicate the number of the cases shown which were aleukaemic.

to 6 females (352 to 295). Acute leukaemia occurred in 142 males and 129 females. In chronic leukaemia there was a male predominance of 210 to 166. The only really impressive sex difference, shown in both series, was in the chronic lymphatic variety, where there were 130 males and 77 females. The sex incidence in the aleukaemic cases was remarkably equal except in chronic aleukaemic myeloid leukaemia, in which eight of the nine cases were female.

Haematological Features

The cases in both series were analysed in respect of the principal haematological findings. These conformed entirely to the expected pattern. The average initial leucocyte counts in the cases of frank leukaemia were as follows: chronic myeloid (160 cases), 237,000 per c.mm.; chronic lymphatic (170 cases), 144,000 per c.mm.; acute lymphatic (89 cases), 84,000 per c.mm.; monocytic leukaemia (40 cases), 72,000 per c.mm.; and acute myeloid (48 cases), 61,000 per c.mm. The two separate series were in close agreement on these figures.

Incidence of Leukaemia

In an attempt to determine whether there had been any real increase in the incidence of leukaemia over the period of the survey, the number of cases of all types detected annually was compared with the total number of admissions to the hospitals in which the cases occurred. This was done in both centres. The results are grouped in seven

TABLE III.—*Biennial Incidence of Leukaemia (All Types) in Hospital Admissions*

Period	Series E		Series A		Combined Series		Incidence
	No. of Cases	No. of Hospital Admissions	No. of Cases	No. of Hospital Admissions	No. of Cases	No. of Hospital Admissions	
1938–9	40	65,000	20	29,337	60	94,338	1/1,572
1940–1	51	59,793	20	27,091	71	86,884	1/1,224
1942–3	41	61,676	18	30,164	59	91,840	1/1,557
1944–5	64	62,353	26	32,455	90	94,808	1/1,053
1946–7	72	67,889	25	37,126	97	105,015	1/1,083
1948–9	91	71,865	50	42,406	141	114,271	1/810
1950–1	81	73,887	48	44,067	129	117,954	1/914

biennial periods from 1938 to 1951 in Table III. Sixty cases occurred in 1938–9, and there was an increase to 90 in 1944–5 and to 129 in 1950–1. Both surveys showed a similar trend. When related to total hospital admissions, leukaemia increased from an incidence of 1 in 1,572 in 1938–9 to 1 in 914 in the period 1950–1.

In both surveys the cases occurring in each two-year period were analysed in respect of the type of leukaemia. These results are given in Table IV, which shows a gradual

TABLE IV.—*Biennial Incidence of Different Types of Leukaemia (Combined Series)*

Period	Acute			Chronic	
	Lymphatic	Myeloid	Monocytic	Lymphatic	Myeloid
1938–9 ..	10 (3)	12 (1)	4 (1)	17 (4)	17 (0)
1940–1 ..	17 (5)	7 (1)	2 (1)	27 (4)	20 (1)
1942–3 ..	13 (3)	6 (1)	6 (1)	17 (2)	17 (2)
1944–5 ..	23 (5)	6 (1)	4 (3)	29 (3)	28 (0)
1946–7 ..	15 (6)	13 (4)	9 (1)	30 (6)	30 (1)
1948–9 ..	29 (16)	16 (9)	18 (7)	47 (11)	30 (5)
1950–1 ..	37 (17)	10 (5)	14 (3)	40 (7)	27 (0)

Figures in parentheses indicate number of cases which were aleukaemic.

but distinct increase in all types of leukaemia, especially in the last four years (1948–51). It will be observed that the increase in the chronic forms of leukaemia was approximately twofold, while the acute varieties showed a somewhat greater increase. The incidence of aleukaemic forms showed a corresponding trend, and, with the possible exception of the acute myeloid variety, there is no real indication of a disproportionate increase in this form of the disease. If the cases of acute and chronic lymphatic leukaemia are taken together the increase is about threefold, while the myeloid forms show a much less striking increase.

Discussion

Perhaps the most interesting feature of this study is the discovery that, in both surveys, chronic lymphatic leukaemia was the commonest type of the disease, and that the relative frequency of the different types was approximately 6 chronic lymphatic to 5 chronic myeloid to 4 acute lymphatic to 2 acute myeloid. This represents a considerable departure from the generally accepted statements that chronic myelogenous leukaemia is the most frequently encountered type of the disease, and that the acute myeloid variety is much commoner than the acute lymphatic (Whitby and Britton, 1950; Wintrobe, 1951). The latter views are certainly supported by most previous reports. A number of these, in which the classification used allows of comparison, are shown in Table V.

The unusual predominance of chronic lymphatic leukaemia in the present series is of much interest, and an explanation is not easily found. It is unlikely that there could have been any significant error in the diagnosis of this, the chronic type of lymphatic leukaemia. A geographic variation in the incidence of types of leukaemia is a possible explanation, and it is true that no large-scale survey of leukaemia in Scotland has previously been made. Indeed, the last major series reported in Great Britain was by Panton and Valentine in 1929 at the London Hospital. A more likely explanation, however, is that there has been a progressive increase in the occurrence of chronic lymphatic

TABLE V.—*Incidence of Different Types of Leukaemia in Published Series*

Author	Total No. in Series	Lymphatic		Myeloid		Monocytic
		Chronic	Acute	Chronic	Acute	
Ward (1917) ..	729	11%	—	34%	—	—
Panton and Valentine (1929) ..	172	14%	N.S.	51%	34%	N.S.
Rosenthal and Harris (1935) ..	455	23%	7%	35%	30%	2%
Leavell (1938) ..	478	27%	N.S.	38%	N.S.	N.S.
Wintrobe (1942) ..	163	33%	N.S.	36%	N.S.	N.S.
Bethell (1943) ..	495	44%		48%		8%
Sacks and Seeman (1947)	154	"Almost equal incidence"				N.S.
Present series (1952)	647	32%	22%	26%	11%	9%

N.S.=Not stated.

leukaemia over the past thirty years, and there is some evidence to support this suggestion. It may be observed from Table V that when the various series reported in the literature are arranged in chronological order there seems to have been a progressive increase in the proportion of the chronic lymphatic type. Furthermore, in the present series, when the biennial incidence of the different types is considered (Table IV), there has been a greater increase in lymphatic forms of leukaemia than any other.

With regard to the striking increase in acute lymphatic leukaemia in this series, as compared with previous reports, it must be admitted that the question of accuracy in diagnosis demands serious consideration. The difficulty of distinguishing the various types of acute leukaemia is well known, and there must be an appreciable margin of error. The likelihood of this error being significant is much reduced, however, when it is observed that there was agreement between series E and A on the proportion of the acute lymphatic group and on its placing in order of frequency. The cases in these two separate series were studied and classified by a number of different observers, and any error due to individual bias in interpretation must therefore have been minimized.

It is difficult to establish from the literature the relative frequency of aleukaemic forms of leukaemia. One source of confusion is the lack of any agreement on definition. Forkner (1938) suggested that aleukaemia (sub-leukaemia) could be defined simply as being present when there was no increase in the total number of leucocytes in the blood, and this definition has been adopted in this survey, accepting 10,000 per c.mm. as the upper limit. Rosenthal and Harris (1935) chose a leucocyte count of 15,000 per c.mm. as the dividing level, and of their 455 cases 23.5% were aleukaemic. On the other hand, the criteria adopted by Bethell (1943) were that at least 10% of leucocytes exhibited an abnormality on which the morphological diagnosis was based, and the total count did not exceed 10,000 per c.mm. Of his series of 495 cases 31.9% were aleukaemic. In the present series the overall incidence of aleukaemic forms was 21.6%. In the different types of leukaemia it was clear that there was a much higher incidence of aleukaemia in the acute forms than in the chronic. Approximately one-third of the cases of acute lymphatic, acute myeloid, and monocytic types were aleukaemic. About one-fifth of the chronic lymphatic cases were aleukaemic, and the lowest incidence was found in chronic myeloid leukaemia, in which aleukaemia was a rare phenomenon.

The observations made on the age incidence of leukaemia in the present study agree on the whole with previous observations. Chronic lymphatic leukaemia (Fig. 1) is shown clearly as a disease of later life (Wintrobe and Hasenbush, 1939). Chronic myeloid leukaemia had a maximum incidence in middle life (Fig. 2). It should be noted, however, that occasional cases may be found below the age of 20, as has been pointed out by Eisenberg and Wallerstein (1934), Keith (1945), and Wintrobe (1951). The age incidence in the cases of acute lymphatic leukaemia followed the expected pattern (Fig. 3), with the maximum incidence in childhood. Indeed, 56 of these cases (38.8%) were children under the age of 5, and 98 cases (68.1%) occurred in the first two decades of life. The disease may, however occur at any age, as was indicated by Kirshbaum and Preuss (1943). In the present series acute myeloid leukaemia occurred over a wide range of ages (Fig. 4) and was by no means confined to childhood. This has also been noted by Bethell. Monocytic leukaemia (Fig. 5) showed a very similar age distribution. Warren (1929) found that about two-thirds of a series of 113 cases of acute leukaemia of all types occurred over the age of 25. Similarly, Kaufmann and Lowenstein (1940) found that a series of 40 acute cases (all types) were almost equally distributed in the first four decades, with a declining incidence thereafter up to the age of 75. The present study would suggest that when acute leukaemias are grouped together the wide range of age incidence is mainly due to the cases of acute myelogenous and monocytic leukaemia.

The findings in regard to sex incidence of leukaemia are of some interest (Table II). Overall, males were more often affected in a ratio of 7 to 6. Rosenthal and Harris (1935) and Sacks and Seeman (1947) found a male predominance of 3 to 2. It has been stated that in chronic lymphatic leukaemia males are affected four times as frequently as females (Whitby and Britton, 1950). Ward (1917), Minot and Isaacs (1924), and Leavell (1938) all reported that about 75% of the cases of this form of the disease were male. In the present study males were affected only twice as often as females. A male predominance has also been reported in chronic myeloid leukaemia (Minot, Buckman, and Isaacs, 1924; Hoffman and Craver, 1931; Leavell, 1938). This was not found in the present series, in which the sex incidence in this type of leukaemia was almost equal. Acute lymphatic leukaemia showed in this series a slight male preponderance (7 to 6), which is not nearly so striking as the position in the chronic lymphatic form. The virtually equal sex incidence in the cases of acute myeloid leukaemia in this series is at variance with previous views (Kirshbaum and Preuss, 1943; Whitby and Britton, 1950). Again, no significant difference was found in the sex incidence in monocytic leukaemia. This is contrary to the report of Osgood (1937) that monocytic leukaemia is twice as common in men as in women.

There is very little information in the literature about the sex incidence in the aleukaemic forms of leukaemia. Table II shows that the overall male predominance of the total series was not reflected in the aleukaemic cases, in which there were 73 females to 67 males. It is interesting to note that in the rare cases of chronic aleukaemic myeloid leukaemia females were in a striking majority.

The question of whether leukaemia is becoming more prevalent or not has exercised a number of authors. Rosenthal and Harris (1935) noted an apparently rising annual incidence, but discarded the idea that there was any real increase in the disease. Powell (1940) and Kirshbaum and Preuss (1943) concluded that the apparent increase was due to improvement in diagnosis. Bethell believed, however, that there had been a real and progressive increase, especially in the acute forms of the disease. Sacks and Seeman (1947), in a comprehensive statistical study, calculated that the disease had almost doubled in incidence in the U.S. over the period 1920–40. They also showed that this increase could not be accounted for by changes in the age distribution of the population at large. It is therefore of much interest to find that leukaemia has increased almost twofold among hospital admissions in 1938–51 (Table III). For reasons already stated it is thought unlikely that there has been any great variation in standards of diagnosis over the period of this survey. This is supported by the results in Table IV, which show that the rise in numbers has affected all types of leukaemia and that there has been no disproportionate increase in aleukaemic forms such as might have been expected if improving diagnosis had been leading to more frequent recognition of the disease.

Further support for the belief that there has been a progressive increase in leukaemia in Scotland during recent

years is provided by the figures published in the Annual Reports of the Registrar-General for Scotland, which are available for the years 1938 to 1949 and which are shown in Table VI. This shows that there has been a gradual rise in the number of deaths from leukaemia during twelve of the fourteen years covered by the present study.

TABLE VI.—*Registrar-General's Reports (Scotland), 1938–49. Deaths from Leukaemia, at All Ages and of All Types*

Year	Deaths from Leukaemia	Year	Deaths from Leukaemia
1938	114	1944	149
1939	108	1945	148
1940	105	1946	168
1941	137	1947	162
1942	129	1948	153
1943	150	1949	201

On these grounds it is suggested that there has been a real and progressive increase in all forms of leukaemia in recent years in Scotland, and, in particular, an increased incidence of the lymphatic type of the disease.

Summary

A review of the features of 647 cases of leukaemia is presented.

This series was obtained by two separate surveys carried out in Edinburgh and in Aberdeen of the cases admitted to hospitals in these centres over the period 1938 to 1951.

Contrary to previous reports, the commonest type was chronic lymphatic leukaemia, followed by the chronic myeloid, acute lymphatic, acute myeloid, and monocytic types, in that order. About one-fifth of the total number of cases were aleukaemic. This phenomenon occurred most frequently in the acute forms of the disease and was least common in chronic myeloid leukaemia.

The age incidence of the chronic lymphatic, chronic myeloid, and acute lymphatic types conformed to the previously reported figures, but acute myeloid and monocytic leukaemia showed a much wider range of incidence than is generally quoted.

Males were more often affected than females, in the ratio of 7 to 6. The male predominance was most pronounced in the cases of chronic lymphatic leukaemia, and was less obvious or was absent in the other types.

Evidence is presented which suggests that there has been a twofold increase in the overall incidence of leukaemia over the period of this survey. There seems to have been a particular increase in the lymphatic type, but all forms of the disease have shown a rising incidence.

We would like to thank the members of the staffs of the hospitals in Edinburgh and Aberdeen for their kind permission to study and publish details of cases under their care. In particular, we are indebted to Professor R. McWhirter for records of many cases seen and treated in the Department of Radiotherapy, Edinburgh Royal Infirmary. Much valuable assistance was given by Professor L. S. P. Davidson and Professor H. W. Fullerton and by the haematological laboratories under their charge in the Departments of Medicine, Universities of Edinburgh and Aberdeen respectively.

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EFFECTS OF GLANDULAR FEVER INFECTION IN ACUTE LEUKAEMIA

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Acute leukaemia is one of the most catastrophic diseases in medicine. Affecting chiefly the younger and middle-age groups, appearing without warning, and giving rise to an acute symptomatology which by its diffuseness indicates the generalized nature of the disease, it has hitherto defied all attempts at treatment. Such agents as deep *x*-ray therapy, drugs such as urethane and the nitrogen mustards, which have their place in the treatment of the chronic leukaemias, are worse than useless in the acute condition, in which their depressing action on marrow elements already gravely affected by the acute leukaemic process is often rapidly lethal.

The folic acid antagonists, of which aminopterin is an example, have been tried and, after the hopes aroused by early reports, have proved most disappointing. The short periods of partial remission which they have certainly produced in a small proportion of cases have been dearly paid for in toxic reactions which in their unpleasant features are excelled only by the acute leukaemic process itself. Blood transfusion in acute leukaemia is of doubtful value and seldom produces more than the most transient improvement. Substitution transfusion had a short vogue, but has nothing to recommend it; it can do nothing that simple transfusion will not also do. Simple transfusion, preferably with fresh blood, is very often performed in acute leukaemia, if only in order to do something. Opinions regarding its value vary. Whitby and Britton (1950) quote Dreyfus, who in reviewing the literature on remissions of acute leukaemia concluded that when such are recorded they have almost always followed the transfusion of blood or plasma. However, this may well be explained by the fact that such a high proportion of all cases of acute leukaemia do, sooner or later, receive transfusions. Wintrobe (1946), on the other hand, considers that, because of the disturbance to the patient and the temporary character of the effect produced, blood transfusion has little justification in acute leukaemia. My view is that, in the absence of distressing symptoms from granulocytopenia or thrombocytopenia, it is most doubtful whether transfusion in itself is valuable, or even humane.

It has seemed to me that, in the study of acute leukaemia and in the search for some effective line of therapy, insufficient attention has been paid to the spontaneous remissions which do from time to time occur, independent of any treatment, and which may last for a few months. Careful study of conditions under which such remissions occur, and search for agents

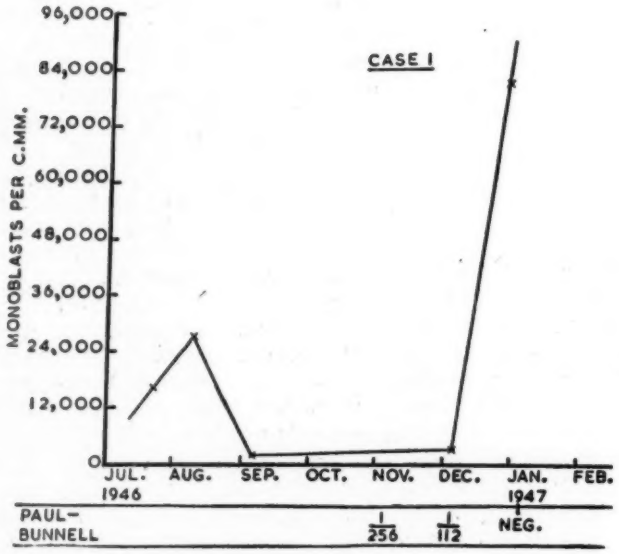
possibly responsible for such remissions, might well be fruitful, and might open the way to completely new lines of attack on this disease.

The part played by intercurrent infections in the induction of remissions—partial or complete—in acute leukaemia is as yet undetermined. At a conference on folic acid antagonists held in America in 1949, and quoted by Dameshek *et al.* (1950), views were put forward by very experienced haematologists that in children suffering from acute leukaemia it is not uncommon for remissions to follow infection, but that similar observations in adults were extremely rare.

The observations recorded here relate to the acute monocytic variety of acute leukaemia and are based on the observation of a clinical remission which occurred in a case of acute monocytic leukaemia in an adult. In this case a remission appeared to coincide with the appearance of glandular fever type cells in the peripheral blood and of a positive Paul–Bunnell heterophil antibody reaction in the serum. In the remaining five cases attempts were made to induce glandular fever infection in cases of acute monocytic leukaemia; the results of these attempts are recorded and their possible significance is examined.

Case 1

A man aged 35 was admitted on July 17, 1946, complaining of intermittent and fleeting pains in the limbs and body for seven weeks, diagnosed as fibrositis. There had been some loss of weight. Increasing pallor had been noticed.



There was a family history of pulmonary tuberculosis. The patient's previous health had been good. On examination there was moderate pallor of the conjunctivae. Small glands were palpable in the neck, axillae, and groins. The spleen was just palpable. The sternum was tender to pressure. No petechiae and no stomatitis were found. An evening rise of temperature to 99.5–100° F. (37.5–37.8° C.) was present and persisted.

The blood picture showed a haemoglobin of 54% (Haldane), 2,200,000 red cells per c.mm., 30,000 leucocytes per c.mm., with 39% monocytes and 12.5% monoblasts. Frequent normoblasts were present. A myelogram confirmed the diagnosis of acute monocytic leukaemia. The patient had a transfusion of 3 pints (1.7 litres) on July 19, but the clinical condition deteriorated. A short course of urethane was given early in August without benefit, and further transfusions of 3 pints were given on August 19, September 7 and 28, and October 8.

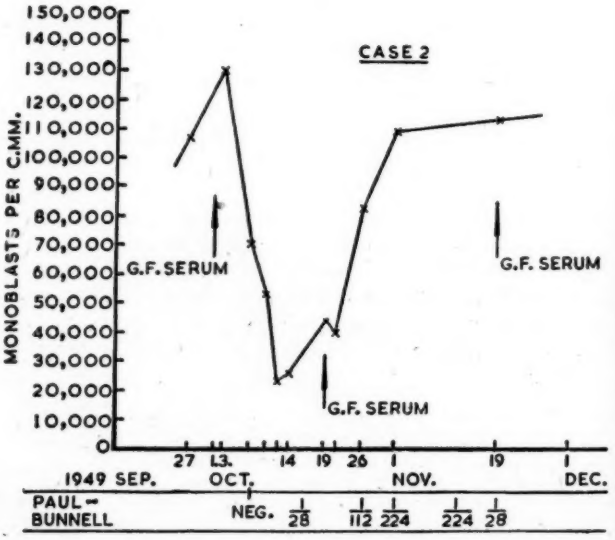
By October 16 he was so much better that he was sent home with a haemoglobin of 74%. The total leucocyte count had fallen to 6,000, with 34.5% of monocytes; no monoblasts were present. There were no symptoms of any sort. He remained well and returned to work. A blood examination made elsewhere early in November showed a haemoglobin of 83%, and the appearances of films at the time prompted the performance of a Paul–Bunnell test, which showed a positive reaction to a titre of 1/256—unchanged after absorption with guinea-pig kidney. Glandular fever was considered as an alternative diagnosis. He was seen in the out-patient department on December 2 and was then apparently in perfect health. Neither spleen nor liver was palpable, there were no glands, and the haemoglobin was 80%. However, the leucocyte count showed clearly that the leukaemic process was still present, and a few monoblasts were seen; small numbers of myelocytes and occasional nucleated red cells suggested a widely disseminated process.

By the middle of December his condition was rapidly deteriorating, and he was readmitted to hospital. The blood picture again showed an acute monocytic leukaemia, with a haemoglobin of 35% and a total leucocyte count of 104,000 per c.mm., 81,000 of which were monoblasts. The liver and spleen were much enlarged. The Paul–Bunnell reaction was negative.

In spite of immediate transfusion the patient died three days after readmission. At necropsy the hepato-splenomegaly was confirmed, and spleen, liver, kidneys, lungs, and all lymphatic nodes showed diffuse leukaemic infiltration.

Case 2

A woman aged 35 was first seen on September 28, 1949. She complained of a few days' acute pyrexial illness with rigors, bouts of abdominal pain, spontaneous bruising of the legs and arms, and increasing soreness and ulceration



of mouth and tongue. Rapidly developing pallor had been noticed. For five months she had had occasional vague dragging pains in the upper abdomen and occasional spontaneous bruising of the legs for five weeks before the onset of the acute illness. She had been a very healthy and athletic young woman, and had had no previous illnesses of any note.

On examination obvious severe anaemia was found, with a slightly icteric tinge. Multiple ecchymoses of varying ages and sizes were scattered over the body and limbs, and a few petechiae were present. There was acute gingivitis with widespread ulceration, and three deep ulcers on the dorsum of the tongue were found. The sternum was tender to pressure. Tachycardia was present, with a soft systolic

murmur at the apex. Her temperature was 103.5° F. (39.7° C.). The spleen was palpable and the liver enlarged. No free fluid was present. A few small soft glands were palpable in both anterior triangles of the neck and a few small shotty glands in the axillae and the inguinal regions. The blood picture showed an acute monocytic leukaemia, with 110,000 leucocytes per c.mm., of which 98% were monoblasts. The haemoglobin was 44% and red cells 1,990,000 per c.mm. Granulocytopenia and thrombocytopenia were pronounced.

The patient was admitted to hospital, and in spite of immediate transfusion of 2 pints (1.1 litres) of blood there was further deterioration with falling haemoglobin and red-cell levels. On October 3 7 ml. of pooled glandular-fever serum from two recent cases of acute glandular fever was given intramuscularly, and 3 pints (1.7 litres) of fresh blood was transfused. Full local and systemic penicillin therapy was employed. Her general condition rapidly improved, and her temperature, which was 104° F. (40° C.) on admission, had settled to normal by October 7. The oral sepsis and ulceration rapidly resolved, haemorrhages ceased, and the abdominal pain disappeared. The patient felt comparatively well. The total leucocyte count fell rapidly to 45,000 by October 13, owing to a fall in the numbers of monoblasts; the granulocytes and lymphocytes increased. The platelets increased to around 100,000 per c.mm. The patient remained fairly well, complaining of nothing except lassitude and occasional slight upper abdominal pain. There was a slight but progressive tendency for the haemoglobin and red-cell levels to fall, but no haemorrhagic tendency and no further oral sepsis.

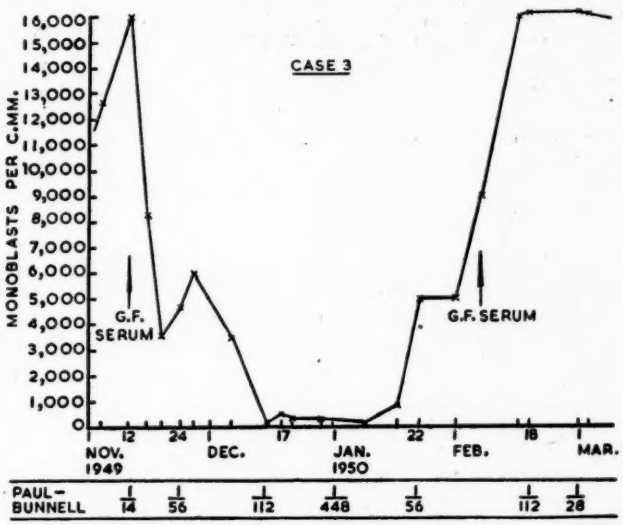
On October 19 5 ml. of fresh glandular fever serum from an acute case was injected intramuscularly. At about the same time a few fresh small glands appeared in the neck in both anterior and posterior triangles. No other glands were enlarged. The spleen remained unchanged in size. Injections of a crude liver extract and full doses of iron were given. By October 26 the haemoglobin was down to 44% and the red-cell count to 2,300,000, and 2 pints (1.1 litres) of blood was transfused. On October 31 the temperature was 100° F. (37.8° C.) and a small ulcer appeared on the side of the tongue; systemic penicillin, which had been discontinued after the first fortnight of the illness, was recommenced and a week's course was given. The ulcer by then had cleared up. The leucocytes were up to 150,000 per c.mm. on November 1, and the haemoglobin was 49%. On November 14 2 pints of blood was transfused, and on November 22 10 ml. of fresh glandular-fever serum was given intramuscularly. Although the patient's general condition remained fairly good, upper abdominal pain became more severe and continuous. There were no fresh signs on abdominal examination, and the source of this severe pain remained obscure.

The patient died suddenly on December 2 without having developed any further haemorrhagic or agranulocytic manifestations.

Case 3

This patient was a woman aged 50 whose previous health had been good and whose medical history revealed nothing relevant. The onset of illness was sudden on October 15, 1949, with symptoms of malaise, pyrexia, lassitude, rapidly increasing pallor, and a severe and increasing stomatitis. Within a few days of the onset subcutaneous haemorrhages and a few scattered petechiae appeared. Small glands were palpable in the anterior and posterior triangles of the neck. The spleen was not palpable. The liver was enlarged and palpable two fingerbreadths below the costal margin. The sternum was very tender to pressure.

The blood picture on November 5 showed a severe macrocytic anaemia, with 20,000 leucocytes per c.mm., including 12,800 monoblasts and 400 myeloblasts, haemoglobin 50%, and red cells 3,620,000 per c.mm. Granulocytopenia and thrombocytopenia were pronounced. By November 9 deterioration was rapid and the temperature was high and



swinging. Next day 3 pints (1.7 litres) of fresh blood was transfused and 5 ml. of fresh glandular-fever serum from an acute case was injected. Full penicillin therapy had already been instituted.

By November 16 both the clinical condition and the blood picture improved, with falls in the total leucocytes to 12,000 and monoblasts to 8,500 and increases in granulocytes and platelets. The stomatitis was clearing up and no fresh skin lesions were appearing. The temperature had fallen to normal, and the patient was feeling better. There was a slow but steady fall in the haemoglobin and red-cell levels. Three pints (1.7 litres) of fresh blood was transfused on December 9, and 2 pints (1.1 litres) on December 31. The patient was now leucopenic, with total leucocyte counts of 1,000–2,000 per c.mm., including 300–700 monoblasts.

On December 24 a small crop of ulcers appeared on the inner aspect of the lips, but these soon cleared up. The patient remained fairly well, though weak, until the end of February, 1950. Early in this month some deterioration in the blood picture was noted. With a rise in the leucocytes to 12,000 and monoblasts to 9,000, and an increase in the anaemia (haemoglobin 53%).

A further 2 ml. of glandular-fever serum was injected on February 6.

At the end of February she had a short but severe attack of abdominal pain with diarrhoea and vomiting, and this left her very exhausted. Her mouth was again becoming sore, and the glands in the neck were larger. Neither spleen nor liver showed any marked increase in size. The deterioration in the general condition became very rapid, and was associated with a very steep rise in the monoblast level and fall in the haemoglobin and red-cell levels. The patient became semi-comatose and died on March 18.

Case 4

A man aged 17 was admitted to hospital on June 7, 1950, complaining of a purpuric skin eruption of recent onset, with pyrexia, sore mouth, and some pain in the region of the right knee. The history was of vague duration—probably extending over the previous three months. On examination there was only slight anaemia. The gums were spongy and hypertrophied, and both gums and soft palate showed the same petechiae which covered the whole body. The spleen was not palpable, but the liver was enlarged and palpable two fingerbreadths below the costal cartilages. The sternum was very tender on pressure. The right knee-joint was a little swollen and painful on movement.

The blood showed a haemoglobin of 78%, red cells 4,020,000, and leucocytes 14,500, with 52% monoblasts. Platelets numbered 20,000 per c.mm. Marrow biopsy confirmed the diagnosis of monoblastic leukaemia. On June 8 4 ml. of a high-titre glandular fever serum was injected

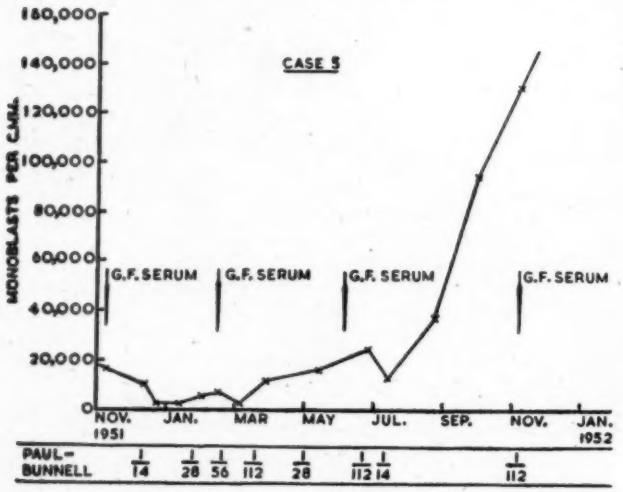
intramuscularly. Paul–Bunnell reactions before and after the injection remained negative and no glandular fever cells were seen in the peripheral blood at any time.

The patient's condition deteriorated and severe epistaxes began on June 18. By June 22 the haemoglobin, in spite of repeated transfusions, had fallen to 38%, the leucocytes numbered 30,000 per c.mm., with 59% monoblasts, and platelets were practically absent. Death occurred on July 10.

Case 5

A woman aged 41 was admitted to hospital on November 23, 1950, with the complaint of a tender painful swelling on the right side of the neck for about four months, with increasing dyspnoea on effort, some loss of weight, spontaneous bruising, and sore throat.

Examination showed a moderate degree of anaemia; there were scattered bruises on both legs, and both spleen and liver were just palpable. On the right side of the neck



there was an irregular glandular mass, involving both anterior and posterior triangles and very tender on palpation. No other glands were palpable. At this time the haemoglobin was 74%, red cells 4,800,000, total leucocytes 32,500, with 36% monocytes and 39% monoblasts. The platelets numbered 135,000. Sternal marrow biopsy confirmed the diagnosis of acute monocytic leukaemia.

While in hospital the patient's condition deteriorated and there was low-grade pyrexia and severe stomatitis. On November 29 4 ml. of a high-titre glandular-fever serum was given by intramuscular injection. During the next six weeks there was a steady clinical improvement. The pyrexia settled, weight increased, and the mass in the neck became smaller. At the same time small rises in both haemoglobin and red-cell levels occurred, the monoblast count fell from 15,000 per c.mm. on November 28 to 3,500 on January 4, 1951, and the total leucocyte count fell from 41,000 to 19,000. The Paul–Bunnell titre rose from an original 1/28 to 1/112 on December 9 and thereafter fell slowly. Small numbers of morphologically typical glandular-fever cells were seen in films following the glandular-fever serum injection, but there was little alteration in the total lymphocyte count.

The patient was discharged from hospital on January 12. Since then she had attended as an out-patient; her condition improved, and she was able to lead a fairly normal life. In February, and again in June and November, further injections of glandular-fever serum were given with subjective improvement on each occasion. Occasional slight stomatitis was controlled by local penicillin. There was no spontaneous bruising and the mass in the neck, though still tender, was neither as large nor as painful as before. The Paul–Bunnell titre rose to 1/112 after each of the glandular-fever serum injections but fell away to 1/14 very rapidly.

The blood picture showed little alteration over the next nine months, with the haemoglobin a little over 70%, red cells about 3,800,000, total leucocytes from 25,000 to 40,000, and monoblasts varying from 6,000 to 28,000 per c.mm. Towards the end of 1951 the leucocyte count rose sharply to over 100,000 per c.mm., including 80–90% monoblasts. There was a parallel deterioration in the patient's clinical condition, and death occurred early in January, 1952, from exhaustion with severe abdominal pain.

Necropsy showed extensive leukaemic infiltration of liver, spleen, kidneys, and lymphatic nodes.

Case 6

A woman aged 35 was admitted to hospital on March 19, 1951, complaining of increasing pallor for two months, repeated epistaxes for one month, severe haemorrhage and stomatitis following tooth extraction three weeks earlier, and severe and continuous bleeding per vaginam since her last menstrual period 12 days before admission.

On admission there was obvious gross anaemia, a severe stomatitis, and a few scattered petechiae on the shoulders and arms. The spleen was not palpable, but the liver edge was just palpable. No glands were enlarged. The blood picture on admission showed haemoglobin, 15%; red cells, 1,980,000 per c.mm.; leucocytes, 6,000 per c.mm., with 23% monoblasts. The platelets numbered 20,000 per c.mm. The M.C.D. was 7.9 μ. Sternal marrow biopsy confirmed the diagnosis of acute monocytic leukaemia.

An intramuscular injection of 2 ml. of a high-titre glandular-fever serum was given. Neither before nor at any time after this injection was the Paul–Bunnell reaction positive, nor were glandular-fever cells seen in the peripheral blood. In spite of massive and repeated transfusions the patient's haemoglobin and red-cell levels fell rapidly, and the uterine haemorrhage continued. Little change took place in the leucocyte total or differential counts. Death occurred from anaemia on April 28.

Discussion

This group of cases of acute leukaemia consists of six cases of acute monocytic leukaemia. In Cases 1, 2, 3, and 5 remissions of varying degree appeared to follow infection by glandular fever; in Case 1 this infection seemed to have been accidentally acquired, and in the other three cases deliberate attempts were made to induce glandular fever by injection of serum taken from cases of glandular fever in the acute stage. Evidence of infection with glandular fever in these cases of leukaemia was provided by the appearance of positive Paul–Bunnell reactions and by the appearance in the peripheral blood of typical glandular-fever cells in varying numbers, accompanied in some cases by transitory glandular enlargement. At the same time in each case there were falls in the total leucocyte counts, the fall being generally due to a sharp drop in the monoblast count. There was a tendency for haemoglobin and red-cell levels to improve and for the platelet counts to rise.

In Cases 4 and 6 there was no evidence whatever of infection following glandular-fever serum injection, and the disease in these cases ran its usual rapid and uninterrupted course.

Attempts to induce glandular fever in two cases of acute lymphatic leukaemia in children have also been made, and the results seem to justify further trial.

Wising (1942) has collected evidence which supports the virus theory of glandular fever aetiology and has described the successful transmission of this infection to man by means of heparinized blood. Bang (1943), in describing unsuccessful attempts to transmit glandular fever to man, suggests plausibly that the method of inoculation and size of dose are less important than the susceptibility of the experimental subject. This may explain the degree of success achieved in this experiment when quite small injections (2–5 ml.) of fresh untreated serum were used.

The manner in which glandular-fever infection might have a beneficial effect on the acute leukaemic process is quite uncertain. The cases of monocytic leukaemia described above were all of the "Schilling" type, which seems to me to bear a distinct resemblance both in its site of origin and in some of its clinical features to the more severe forms of glandular fever. The large type of glandular-fever cell seen in the first few days of acute glandular fever bears a close resemblance to certain of the leukaemic monocytes, although the mature cell of glandular fever is quite unlike any variant of the leukaemic monocyte or monoblast. It is possible that infection by the benign condition exerts a diversionary influence on the malignant leukaemic process.

It would be obviously most unwise to draw any sweeping conclusions from this very small series of cases. It does seem, however, that the clinical and haematological results obtained are more than can be explained either by the blood transfusions which some of the patients received or by chance.

It is suggested that further trial of the effect of induced glandular fever in cases of acute monocytic leukaemia is justified. It is even possible that in suitable cases the effects might be more profound and lasting than in those described.

Summary

Observations on the effect of glandular fever infection, natural and induced, in cases of acute leukaemia are recorded. It is concluded that there is evidence that such infection may in some cases be responsible for remissions in leukaemic disease.

Thanks are due to Dr. B. B. Hosford and Dr. J. M. Ranking for their co-operation, to Professor G. Payling Wright for helpful criticism, and to Dr. C. J. C. Britton for two batches of the glandular-fever serum used.

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MONOCYTIC LEUKAEMIA PRESENTING AS POLYARTHRITIS IN AN ADULT

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Leukaemia presenting as acute polyarthritis is common in children but rare in adults. There is no agreement about the pathological cause of this joint involvement, so the following case, in which an infected joint was examined histologically, is reported.

Acute rheumatism and leukaemia have been reported as occurring together by Ehrlich and Forer (1934). Uncomplicated leukaemia presenting as acute polyarthritis has been described by many authors, and its rarity in childhood was stressed by Bichel (1948) and Baldridge and Awe (1930). A few adult cases have been recorded by Seward (1930), Barney (1933), Henschen and Jezler (1935), and Wintrobe and Mitchell in 1940, and the whole question of bone and joint lesions in acute leukaemia has been reviewed by Dresner (1950).

Case History

In February, 1950, a 39-year-old police constable developed a febrile illness diagnosed as measles. In the following three months he lost nearly a stone (6.4 kg.) in weight and complained of fleeting pains in different joints. No abnormality was seen in a chest *x*-ray film, so he was referred by his doctor to a physiotherapy department. *X*-ray examination of the spine and pelvis showed no abnormality, but an E.S.R. of 77 mm. in the first hour (Westergren) and a normocytic anaemia with Hb 66% (9.8 g.%) were found. The leucocytes totalled 5,000 per c.mm., with a normal differential count. At the end of May his elbows, knees, and left ankle became swollen, and he began to sweat excessively. He was referred to a surgeon, and thence to hospital. He was admitted on June 14 with a provisional diagnosis of acute infective arthritis.

On examination he was found to be a pale, thin, excitable, and self-depreciative man, with a moderate pyrexia and accompanying tachycardia. His tongue was furred and the fauces were inflamed. One small lymph node was palpable in each axilla. Both knees and both ankles were swollen and tender, and the left elbow, though not swollen, was painful on movement. There was no other physical abnormality. The urine contained a small amount of albumin but no other abnormal constituents. The E.S.R. was 72 mm. in the first hour (Westergren). The Hb was 56% (8.3 g.%) and slight anisocytosis was present. The leucocytes totalled 5,000. Routine agglutination tests were all normal and blood culture was sterile. *X*-ray films of the chest and ankles showed no abnormality.

During the next 14 days systemic penicillin and sodium salicylate were given in doses large enough to produce symptoms of salicylism and a serum salicylate level of 40 mg. per 100 ml., but his fever and flitting joint pains continued. The E.S.R. rose to 140 mm. in the first hour, and 18 days after admission his Hb had dropped to 46% (6.8 g.%) with 2,800,000 erythrocytes. The leucocyte count remained at 5,000 (polymorphonuclears 50%, lymphocytes 43%, monocytes 7%, and an occasional nucleated erythrocyte).

Two days later he became extremely ill. The E.S.R. was 150 mm. in the first hour, the Hb fell sharply to 34% (5 g.%), while the leucocytes increased to 5,800. At this stage a diagnosis of acute aleukaemic leukaemia was considered and a sternal marrow puncture was performed, but a satisfactory marrow specimen was not obtained. An intravenous infusion of 4 pints (2.3 litres) of packed red cells was given, and this temporarily raised the haemoglobin percentage without improving the patient's general condition.

On July 9 the tonsils and some cervical and inguinal lymph nodes became enlarged, but a chest *x*-ray film showed no enlargement of hilar nodes. Haemorrhages appeared in the retinae and palatal mucosa. The leucocyte count was 10,000 (polymorphonuclears 50%, lymphocytes 41%, monocytes 9%). Next day the leucocytes rose to 12,000 and the film showed abnormal mononuclear cells. Sternal puncture was again unsuccessful. By July 12 the Hb was 48% (7.2 g.%). The leucocyte count was 13,800 (stem cells 9%, monoblasts 20%, promonocytes 34%, monocytes 11%, lymphocytes 12%, neutrophil polymorphs 13%, plasma cells 1%). There was one nucleated red cell per 100 leucocytes. Next day the total leucocyte count had risen to 17,000. The picture was thought to be that of acute monocytic leukaemia.

By this time the patient was prostrated, with a swinging temperature and severe dyspnoea. Both ankles were swollen and there were effusions in both knee-joints. There was generalized lymph-node enlargement and the liver was felt three fingerbreadths below the right costal margin. The spleen was not palpable. Several small hard nodules were felt in the scalp. During the next few days the glands became bigger and the spleen became palpable three finger-

breadths below the ribs. Oedema of the ankles appeared. The haemoglobin percentage fell to 26% (3.8 g.%) and the total leucocyte count to 10,600. Death occurred on July 20.

Relevant Necropsy Findings.—The skin and all organs were pale, with many petechial haemorrhages. Several tough, pale nodules were present in the scalp, and there was a large haematoma on the extensor surface of the right forearm. The lymph nodes were all enlarged and pale. The spleen was enlarged, weighing 26 oz. (737 g.). On section it was red, soft, and coarsely granular. The liver weighed 92 oz. (2,608 g.), and was pale and firm on section. The right ankle-joint was opened. The synovial membrane, synovial fluid, and articular cartilage looked normal.

Report on Histology.—"Sections of liver, spleen, lymph node, scalp nodule, skin haematoma, kidney, and small intestine show, in greater or less degree, infiltration by immature leukaemic cells. A portion of the synovial membrane of the left ankle shows infiltration by leukaemic stem cells. The cells have round or ovoid vesicular nuclei and a thin rim of poorly staining basophilic cytoplasm. The cells are especially densely packed in a synovial villus and tail off into the deeper layers between the perisynovial fat cells."

Discussion

In a review of the joint lesions complicating acute leukaemia Dresner states that "little has been written about the pathology of the joint lesions in leukaemia." The cause has been variously suggested as leukaemic deposits in the metaphysis (Bichel), haemorrhage in the joint (Baldridge and Awe), and haemorrhage in the articular surfaces (Conybeare, 1936), but in most of the few cases in which the joints themselves have been examined no significant changes have been found (Wintrobe and Mitchell, Bichel). Dresner reports a case in which the synovium was extensively infiltrated by leukaemic deposits, and concludes that "such leukaemic synovitis is presumably responsible for many of the joint symptoms of leukaemia."

In our case the synovium of an ankle-joint looked normal at necropsy, but was found on histological examination to be infiltrated by immature leukaemic cells. No evidence of leukaemic deposits in the metaphyses was shown by *x*-ray films. The articular cartilage was macroscopically normal, although unfortunately it was not examined histologically. The scalp nodules were an interesting feature of the case. Poynton and Moncrieff (1929) reported two cases of children with fever, pain, swelling in joints, and subcutaneous nodules in the scalp. Their patients also had enlarged livers, spleens, and glands, and progressive anaemia with terminal haemorrhages. They quote a third similar case. All three cases had a "mononuclear response in the blood."

Summary

A case of acute monocytic leukaemia in an adult is described. It presented as a febrile polyarthritis. Post-mortem examination showed leukaemic infiltration of the synovium of a joint.

We should like to thank Dr. T. A. J. Wickham for his histological report.

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An aural microscope designed by Mr. C. S. Hallpike, director of the Medical Research Council's Otological Research Unit, has been adapted for chick sexing. It was originally made to facilitate delicate operations within the ear. The National Research Development Corporation is bearing part of the initial production costs of making the instrument for the poultry trade.

MASS TREATMENT OF TREPONEMAL DISEASES, WITH PARTICULAR REFERENCE TO SYPHILIS AND YAWS*

BY

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Syphilis, yaws, bejel, pinta, and similar conditions caused by treponemes are responsible for various acute and chronic pathological conditions resulting in incapacitation and invalidism of considerable social and economic importance throughout the world. Since these diseases, caused by *Treponema pallidum, T. pertenue, T. carateum,* and other closely related micro-organisms, constitute a group of related infections, an increasing number of investigators[1 2 3 4 5 6 7] are calling for a comprehensive world view of treponematoses rather than a narrow approach based only on the mode of transmission or on minor variations in the resultant clinical syndromes.

Venereally acquired syphilis is prevalent, to a greater or less extent, in all parts of the world, including highly developed countries and communities. There have also been recognized in recent years a number of important geographical "pockets" of treponemal infections, clinically identical to syphilis but epidemiologically similar to yaws. Among them are the "endemic" syphilis of Bosnia, Yugoslavia,[8 9] Madras, India,[10] Bechuanaland, South Africa,[11] and Tahiti in the South Pacific,[12] as well as the "njovera" of Southern Rhodesia.[13] These are examples of non-venereally transmitted communicable treponemal disease in children. "Bejel" is also a non-venereal treponemal infection[14 15] transmitted by direct and indirect contact among children in the Eastern Mediterranean area, particularly in Syria, Iraq, and neighbouring countries. Of even greater importance, however, are tropical framboesia (yaws) and pinta, which affect millions of children and adults in tropical and semi-tropical areas. (In Indonesia alone there were, until recently, an estimated 10 million cases of yaws[7] and in middle America it is estimated that a million or more cases of pinta exist.)

It is unfortunate that, in the areas of the world where mass serological testing would reveal the highest incidence of cases, the facilities for serodiagnosis are the least adequate. For example, whereas sample serological surveys in Saskatchewan, Canada, have shown only 0.25%, of positive readings,[16] in Bergen, Norway, 0.61%,[17] and in London, England, 0.67%,[18] on the Gold Coast of Africa as much as 50%,[19] in Haiti 39%,[20] and in India 25–30%[21] of non-negative serological reactors have been found in various population groups tested.

*Presented before the Tenth International Congress of Dermatology and Syphilology, London, July, 1952.

As the establishment of adequate diagnostic facilities in the undeveloped areas will take several decades to achieve, it is our view that, where necessary, mass treatment can and should be effectively carried out on a large scale before complete facilities have been made available. In undeveloped countries there is an obvious immediate need for a simple and reliable inexpensive screening test which will give a minimum of false positive results.

The availability of a safe and effective therapeutic agent, penicillin, in place of the toxic arsenicals; the simplification of administration of this antibiotic by the development of repository preparations; the development of methodology, making possible a greater understanding of the biology of the treponematoses—have all contributed in recent years to the delineation of a more rational concept of and approach to the control of treponemal infections.

The United Nations World Health Organization, with the aid of supplies and equipment provided by the International Children's Emergency Fund, has embarked on a broad programme of treponematosis control in support of those national health organizations that have requested assistance. In these projects, which have been in operation for less than three years, more than nine million people have been examined, and over three million of these have been treated with penicillin. In Table I are shown the numbers of persons examined and treated up to December, 1952, in six of the larger programmes.

TABLE I.—*Persons Examined and Treated in Six of the Larger W.H.O./U.N.I.C.E.F.-supported Treponemal Disease-control Programmes*

Programme	No. Examined	No. Treated
Haiti (yaws)	2,270,051	2,270,051
Indonesia (yaws)	3,529,831	533,587
Thailand (yaws)	1,679,342	216,047
Philippines (yaws)	415,000	24,000
Iraq (bejel)	88,299	29,433
Yugoslavia (endemic syphilis) ..	1,472,402	90,235
Totals	9,454,925	3,163,353

Therapeutic Aspects of Mass-treatment Programmes

In laboratory investigations carried out at the W.H.O. International Treponematoses Laboratory Centre, Baltimore, U.S.A., where some twenty different strains of treponemes from many W.H.O.-supported control programmes are now being maintained in animals, Turner[22] noted that it has not been found possible to demonstrate any consistent variations in the penicillin sensitivity of treponemes isolated from active cases of venereal and non-venereal syphilis. The actual results obtained by therapy confirm the justification of the approach to the treponemal diseases as a group, and it is now an established fact that penicillin is highly efficacious in all of the treponematoses.[3 23 24 25 26 27 28 29 30 31 32 33 34] There are a number of practical considerations which favour the use of repository penicillin preparations which give plasma penicillin levels of long duration with a single or few injections. The practical effectiveness of such preparations is shown in Table II.

It is a basic consideration that the concentration of penicillin in tissue fluids is reflected in the plasma, and that its concentration in circulating plasma bears a definite relationship to its presence at the site of infection. Various methods have been devised to correlate the plasma concentration and its treponemicidal effect. Among microbiological methods the agar-plate and nutrient-broth techniques are the more popular. A number of test organisms are used, but *Sarcina lutea* has been accepted as a standard by W.H.O. for comparative studies.

TABLE II.—*Outcome of Penicillin Treatment in Treponemal Disease. Procaine Penicillin in Oil with 2% Aluminium Monostearate (P.A.M.)*

Infection	No. of Patients Followed	Schedule (Units of P.A.M.)	Period of Follow-up	Clinically and Serologically Satisfactory
Venereal syphilis (primary and secondary)[35*]	102	1·2 million (single injection)	12 days	88·2%
Venereal syphilis (secondary)[35]	29	,, ,, ,,	24 months	72·6%
,, ,, ,,	15	2·4 million (single injection)	24 ,,	84·2%
,, ,, ,,	38	4·8 million (1·2 million in 7 days)	24 ,,	86·6%
Endemic syphilis (early infectious stages)[36]		3·6 million (6 × 600,000)	24 ,,	95·5%
Bejel (early infectious stages)[24]	89	1·2 million (single injection)	7 ,,	92·5%
Yaws (early infectious stages)[24]	312	1·2 million (4-day schedule)	12 ,,	95%
,, ,, ,,	314	1·2 million (2-day schedule)	12 ,,	94·4%
,, ,, ,,	161	2·4 million (4-day schedule)	12 ,,	96·2%
Pinta (primary, secondary and late)[37]	214	1·2 million (single injection)	24 ,,	83·9%
,, ,, ,,	118	1·2 million (300,000 units at weekly intervals)	24 ,,	84·3%

* Includes 18·6% treated with 2·4 million units of P.A.M.

The determination of the dosage of penicillin to be used in mass treatment is an eminently practical point. The number of failures is roughly proportional to the duration of an effective plasma level of penicillin, and thus inversely proportional to the cost per patient treated. As penicillin is one of the most expensive expendable items of a mass-treatment programme, the decision regarding dosage must be a "calculated risk," a compromise between maximum therapeutic efficiency and administrative expediency. The W.H.O. Expert Committee on Venereal Infections, with these factors in mind, recommended that field teams consider an initial injection of 1.2 million units of procaine penicillin G in oil with 2% aluminium monostearate, and then, if feasible from the standpoint of field operations, a further injection may be given at an interval of three to five days.

The penicillin preparations used should (*a*) result in the longest possible effective plasma levels, (*b*) be effective with the smallest possible amount injected, and (*c*) cure a high proportion of infectious cases. The recommendations of the W.H.O. expert committee are predicated on the use of preparations of P.A.M. that consistently maintain effective plasma levels for several days following a single injection of 1.2 million units[35 38] (Fig. 1).

Unfortunately it has been the experience of W.H.O. that there are very great differences among P.A.M. preparations

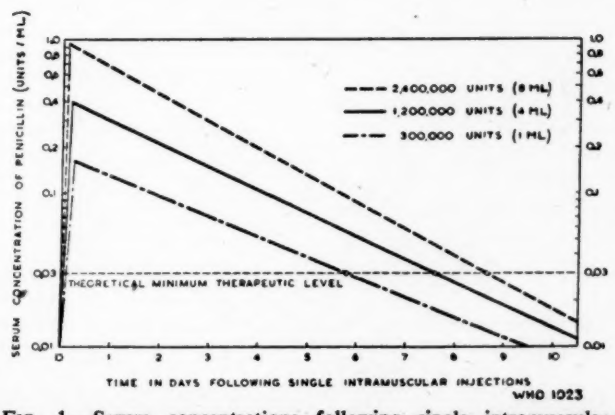
SERUM CONCENTRATION OF PENICILLIN (UNITS / ML.)
2,400,000 UNITS (8 ML)
1,200,000 UNITS (4 ML)
300,000 UNITS (1 ML)
THEORETICAL MINIMUM THERAPEUTIC LEVEL
TIME IN DAYS FOLLOWING SINGLE INTRAMUSCULAR INJECTIONS
WHO 1023

FIG. 1.—Serum concentrations following single intramuscular injections of procaine penicillin G in oil with 2% aluminium monostearate.

in their ability to maintain plasma penicillin concentrations necessary for mass campaigns based on schedules involving one or few injections. Numerous samples of P.A.M. preparations produced in different countries by different manufacturers have therefore been analysed with particular reference to the duration of effective plasma concentrations by means of the *Sarcina lutea* technique used by the United States Food and Drug Administration Antibiotics Laboratory (Fig. 2).

It will be seen that, while some products show effective blood levels after 72 to 96 hours (based on assays of at least 10 ambulatory patients), no trace of penicillin is detectable in the plasma of others after 24 hours. *Thus the need for the proper standardization of P.A.M. preparations is apparent,* and to meet this need W.H.O. has recently established certain minimum specifications that are acceptable for field work in W.H.O. treponemal disease-control programmes. These minimal specifications are being included

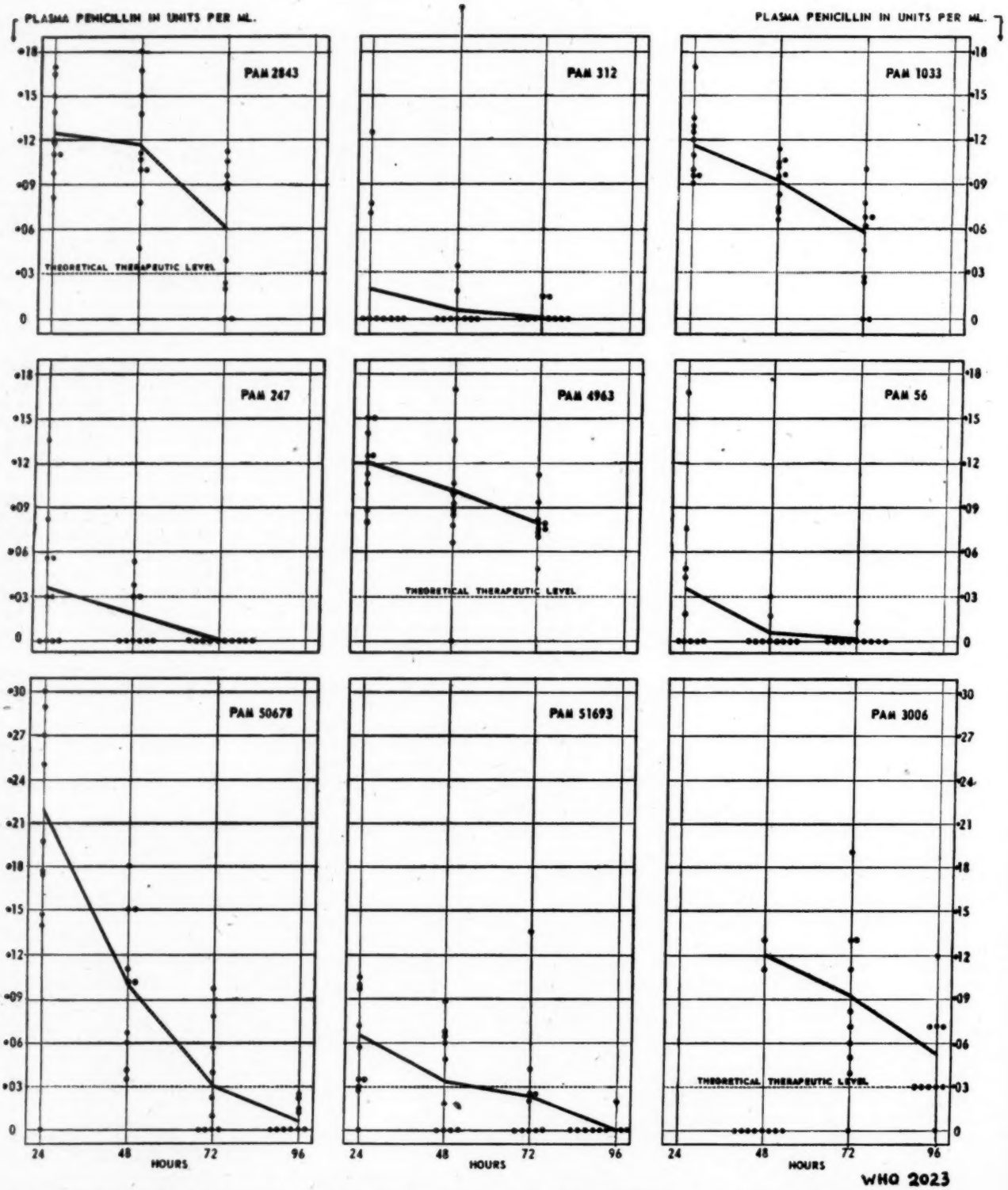

FIG. 2.—Varying efficiency of P.A.M. preparations. Plasma penicillin concentrations (*Sarcina lutea* technique) following intramuscular injection of 300,000 units procaine penicillin G in oil with aluminium stearate (P.A.M.) of different manufacture. Mean arithmetic value of observations and their spread based on at least 10 ambulant persons tested at each time interval indicated.

in the second volume of the *International Pharmacopoeia*. The most important is that an intramuscular injection of 1 ml. (300,000 units) into humans should maintain a penicillin concentration in the blood of not less than 0.03 unit per ml. (*Sarcina lutea* technique) for 72 hours in the majority of subjects. It is also stated that at least 65% of the particles must be 5 μ or less as determined by microscopical chamber counts, that when shaken the emulsion should be stable for 48 hours with a layer of oily separation not exceeding 3 mm., and that the preparation should pass easily through an 18-gauge needle.

Epidemiological Aspects of Mass-treatment Programmes

The approach to mass treponemal-disease control by therapy is one by which it is sought to reduce the level of infectiousness in a given area to a point where it can be successfully managed despite the limited facilities available in the underdeveloped countries. Five important programme stages are outlined[6]: (*a*) orientation and preliminary analysis of the problem; (*b*) development of methods; (*c*) demonstration and survey phase; (*d*) expansion phase (mass treatment); and (*e*) consolidation of the programme.

While the general response of a population group to a planned regimen can be forecast in broad terms on the basis of available knowledge, its actual effect in detail can be assessed only on the basis of the findings in a control or pilot area. In these areas control groups can be studied with the aids of technical laboratory refinements, and the lessons learnt may then be applied to the broad mass as a whole.

There is ample evidence that mass treatment of clinically diagnosed disease in the early stages alone does not suffice, and that supplementary long-term measures are necessary. Thus Harding, in Sierra Leone,[37] established beyond question the importance of consolidating the initial gains in large-scale programmes by establishing a proper follow-up mechanism involving permanent facilities to control reinfections, relapses, and the reintroduction of the disease from outside the area (Table III).

TABLE III.—*Outcome* of Yaws Campaigns in Sierra Leone Following Mass Therapy With and Without Follow-up Measures (Modified from Harding)*

	1941	1942	1943	1944	1945	1946
Mass treatment only	13·7	5·8	—	7·5	—	—
Mass treatment plus permanent treatment facilities	—	5·8	—	3·0	1·8	—
Mass treatment and permanent facilities plus home visits ..	—	—	—	3·4	0·6	0

* All rates are expressed as percentage prevalence of infectious yaws among sample population groups.

Although the emphasis is placed on the control of the infectious cases of treponemal disease this should not preclude the treatment of disfiguring and incapacitating late manifestations, or the discovery and treatment of latent cases which, if left untreated, might serve as foci of further spread. Other important considerations are:

(*a*) *Abortive Treatment of Contacts.*—The "prophylactic," "preventive," or "abortive" treatment of persons who have been immediately exposed to infectious treponemal disease, and who may be incubating the infection, is a question on which medical outlook differs in various parts of the world. Following the demonstration by Alexander and Schoch[38] of the almost complete protection which may be afforded by penicillin to the contacts of venereal syphilis, many American workers consider that persons so exposed should be treated before the disease becomes manifest. This view is gaining support also in South America, the Far East, and Europe, notwithstanding the fundamental changes in outlook and attitude that involves in the medical profession. There can be little doubt that the abortive treatment of contacts is an effective epidemiological procedure, since it helps to shrink the reservoir of infectiousness and to slow the spread of infection in the population generally, especially if applied on a large scale. In the yaws control programme in Haiti, household contacts of yaws cases have been treated with P.A.M., and those who have observed the programme[39 40 41] are convinced of the value of this procedure, it being extremely difficult to find a case of infectious yaws in the control areas where the method has been used. Similar experiences are accumulating in the endemic syphilis programme in Yugoslavia.

(*b*) *Desirability of Examining the Entire Population.*—It is obvious that examination of 100% of the population can seldom be achieved. On the other hand, available evidence suggests that the results will fall below expectation unless a high proportion, approximately 90%, are examined in the initial survey. A recent study in Haiti indicates that if case-finding relies solely on voluntary attendance at permanent clinics, even when suitable propaganda machinery is used, less than 50% of the population will be reached. If, in addition, mobile clinics are held in strategic areas the yield may be increased to almost 70%, but if a house-to-house canvass is substituted the yield will be 91% or more.[41]

(*c*) *Necessity for Re-checks Following Mass Treatment.*—A recent monograph by Grin[42] describes the successful organization and administration of a large-scale programme against endemic syphilis in Bosnia. It is evident that if follow-up measures are deferred for too long—for more than six months to a year, depending on local conditions—a significant number of new infectious cases will almost invariably be found (Fig. 3). In a village of a population

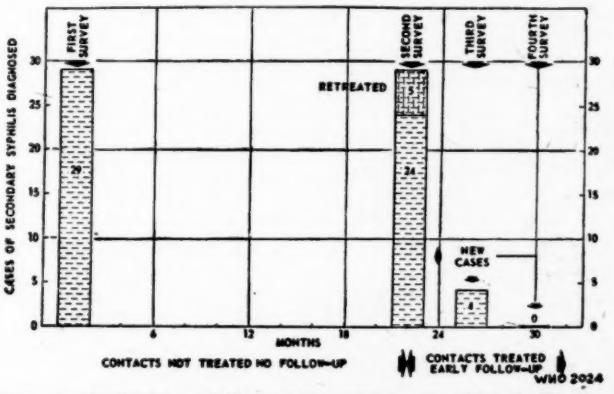

FIG. 3.—Endemic syphilis control programme, Trnaci, Bosnia. Results of revisiting an area at varying time intervals. Entire population (573) examined on all surveys. Syphilis prevalence: secondary 29, latent 88, tertiary 11; total 128 cases (22%).

of 573, 29 cases of secondary syphilis were found when the initial case-finding and mass-treatment programme was launched in August, 1948 (first survey). The second survey, when the entire population was again re-examined, was deferred for 22 months, and, although only five cases of infectious syphilis (? reinfections) were found among those originally treated, 24 additional cases were detected in the remaining population—as high a total incidence as at the beginning. All cases and all household contacts were then treated, and a third survey was made only four months later, when four more cases of infectious syphilis were found, none of which were in those previously treated. These and their household contacts were then treated, and a fourth survey carried out two months later, 30 months after the first survey, revealed no infectious case of syphilis. The village was still free from endemic syphilis in November, 1951.

(*d*) *Necessity of Re-examining the Whole Population on Re-survey.*—The example given in (*c*) serves to emphasize this point. Similar experiences have arisen in the Indonesian programme. Approximately 85% of the infectious cases discovered when the villages were re-examined would have been missed if the group originally treated had been the only one studied.

In its future work W.H.O. will be guided by these important observations, and it is believed that the results of mass-treatment campaigns will be improved thereby. The ultimate success, however, must depend on how the gains achieved by the mass-treatment campaigns are consolidated by the expanding health services of the local health administrations.

Conclusions

Recent advances, particularly the development of effective "one-shot" or "few-shots" forms of therapy with P.A.M. (procaine penicillin in oil with 2% aluminium monostearate) have made possible rational and more readily carried out mass campaigns against the treponemal diseases. In these campaigns there is an important role for international organizations such as W.H.O. and Unicef.

To make comparative evaluation studies possible, and to be fully effective in large-scale campaigns, preparations of P.A.M. must give prolonged serum concentrations. Constant vigilance is necessary to ensure that suitable preparations are used, since there are enormous differences in the products available in different countries to-day.

In carrying out mass treponemal disease-control campaigns it is desirable to maintain primary control areas in which serological tests are used systematically. In the broader programme it is necessary to have as full a coverage of the population as possible and to treat routinely the contacts of infectious cases.

Mass treatment alone is not enough. The gains obtained by mass therapy must be firmly consolidated. In order to do so, re-surveys of the entire population should be carried out at periodic intervals, which should be not less frequent than 6–12 months for several years.

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PROGUANIL AND BLACKWATER FEVER

BY

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Proguanil, unlike quinine, pamaquin, and to a lesser extent mepacrine, has not been known to precipitate blackwater fever when administered to malarial patients. Two cases following its use are therefore worth recording.

Case 1

A civilian aged 20 was admitted to a military hospital on November 1, 1949. He hailed from the Punjab, and had entered a locally endemic area about nine months previously. There was no history of malaria, but symptoms suggestive of latent malaria were present for about three months before admission.

At the time of admission he had been suffering from malarial agues for two days. His temperature was 101–103.8° F. (38.3–39.9° C.), pulse 80–96, and respirations 20–26. His blood showed a few M.T. rings. He was put on a routine proguanil course of 200 mg. thrice daily for two days, followed by 100 mg. thrice daily for eight days. The response to proguanil was good, and next day there was profuse sweating and his temperature started falling. After 800 mg. of the drug had been administered he had repeated rigors again and passed 240 ml. of characteristic very dark haemoglobinuric urine. He felt sick and vomited thrice, and then followed prostration, giddiness, diminished vision, and palpitation on slight exertion. His blood pressure was 110/70 mm. Hg. There was pain in the loins and urgency to micturate, but only a few drops of urine were passed, sometimes none. Temperature 99.4° F. (37.4° C.), pulse 106, and respirations 24.

Laboratory Investigations.—Urine : heavy cloud of albumin, trace of sugar, considerable amorphous deposits, and few hyaline casts, and Hb spectroscopically. Blood : Hb, 60% (Sahli) ; red cells, 3,200,000 per c.mm. ; white cells, 13,900 per c.mm. (polymorphs 54%, lymphocytes 40%, mononuclears 4%, eosinophils 2%). Blood urea, 43 mg. per 100 ml. ; urine urea, 4.9 g. per 100 ml. Blood slides negative for malaria parasites ; serum positive for oxyhaemoglobin and methaemoglobin (methaemalbumin not tested for) ; blood collected for serum bilirubin haemolysed ; total serum proteins, 7.2 g.% (albumin 4 g.%).

Alkalis at the rate of 120 gr. (8 g.) in 24 hours were given by mouth and 3 pints (1.7 litres) of 5% glucose-saline was given in 12 hours by intravenous drip. In about 24 hours there was no vomiting, and the urine, which had begun to be passed in increasing quantities, showed signs of progressive clearing. The patient, however, had another but milder rigor and the urine became darker again. An intravenous injection of 20 ml. of concentrated (anti-snake) antivenene was given to prevent further haemolysis. Next day diuresis

set in and the urine cleared rapidly. Subsequently the average daily urine output was 2.91 litres against an intake of 3.24 litres, and the general condition improved concomitantly. Increased urobilin was present in the urine for five to six days, and a few M.T. gametocytes were found in the peripheral blood on daily examination. On the eleventh day the patient was up and about and feeling all right. His Hb was 70%, red cells 3,890,000 per c.mm., and the urine normal except for a trace of albumin. On the fourteenth day he was discharged.

Case 2

A man aged 30 was admitted to a military hospital on September 17, 1952. He had taken 600 mg. of proguanil on his own for an attack of malaria, and had developed a mild attack of blackwater fever about 8½ hours later. He was a Punjabi and had been in the locally endemic area for about a year. His last attack of malaria occurred in the North-west Frontier Province in 1942.

On admission he complained of fever with rigor since noon that day, and headache, weakness, and lumbar pain since about eight and a half hours after taking proguanil. Two hours later he vomited twice and then passed a small quantity of urine, but did not notice anything abnormal about it in the darkness of the night. About six hours later in the morning he passed about 4 oz. (114 ml.) of dark haemoglobinuric urine. Urine was passed in increasing amounts subsequently and cleared in about 24 hours. No facilities were available here to do any special examinations. A routine urine deposit examination, however, proved that the case was not one of haematuria and a blood examination showed B.T. rings.

Four days later, when the patient was received at the main hospital, the serum bilirubin was 0.4 mg. per 100 ml., both serum and urine were negative for oxyhaemoglobin and methaemoglobin, but the urine was positive for urobilin in 1 in 80 dilution. The blood count was about normal. A few B.T. gametocytes were present in one sample of blood. Treatment consisted of adequate quantities of alkalis and fluids by mouth.

Discussion

It is an undisputed fact that blackwater fever sometimes develops in endemic areas in individuals who have never taken any antimalarial drug. Although it is malaria which is the chief factor in the aetiology of blackwater fever, any antimalarial drug can, however, be a precipitating factor, quinine being the most dangerous of them all. The exact mechanism by which they precipitate the disease is not known. But in relation to current theories regarding mechanism of haemolysis in blackwater fever the following are the possibilities.

1. *Blackwater fever is a sensitization reaction to proteins of malaria parasites. Antimalarial drugs destroy malaria parasites and liberate proteins which are required to precipitate a haemoclastic crisis.*—Increased haemolysis seems to be a natural process during the acute stages of malarial infection, as shown by increased serum bilirubin figures obtained by several workers. The haemolysis bears no relation to the degree of infection, and lighter infections may be associated with heavier bilirubinaemia, but apparently it is heavier in cases with splenic enlargement. The parasite is therefore not directly responsible for the haemolysis. Plehn (1936) suggested that the red blood cells become hypersensitive to the proteins of the malaria parasites which are liberated, with their repeated destruction during each attack of clinical malaria, and that a stage in hypersensitiveness is finally reached when the liberation of a little of this protein precipitates the haemoclastic crisis of blackwater fever.

Fernán-Nuñez (1936) assembled evidence in support of Plehn's theory. He found that 16 out of 410 individuals who had lived in an endemic area for six months or more and who had suffered from M.T. malaria were sensitive to an antigen prepared by him from malaria parasites, and that blackwater fever did not occur when these individuals were removed from the site. More recently, Findlay and Markson (1947), with their experience of troops in Africa, have again suggested that sensitization to the malaria parasite is an essential cause of haemolysis in blackwater fever. However, although all antimalarial drugs destroy malaria parasites, and red blood cells containing them constantly undergo lysis and must liberate this hypothetical haemolytic substance, quinine is the most predisposing drug. Hence such a sensitization reaction alone cannot explain the haemoclastic crisis of blackwater fever.

2. *Blackwater fever is the result of autohaemolysins. These autohaemolysins can accumulate in the spleen and can be thrown out into the general circulation by the contractile action of antimalarial drugs on the spleen. Antimalarial drugs also help in the production of autohaemolysins.*—Gear (1946) has suggested an explanation for the origin of haemolysins in blackwater fever. On the analogy of experimental evidence obtained by him and by Schwentker and Comploier (1939) he thinks that red blood cells infected with malaria parasites become auto-antigenic and give rise to haemolytic auto-antibodies in the reticulo-endothelial system. The haemolytic auto-antibodies sensitize red blood cells, infected or non-infected, and the sensitized cells can undergo haemolysis in the presence of the complement. He further suggests that antimalarial drugs may help in the production of auto-antigens.

The works of Barcroft (1920), Knisely (1934), Fåhraeus (1939), and Ham and Castle (1940) suggest that the spleen is an ideal place for sensitization of red blood cells described by Gear. The haemolytic auto-antibodies over and above those required to sensitize red blood cells in the spleen accumulate there and can be thrown out into the general circulation when the spleen contracts. A haemoclastic crisis may then follow. It is interesting to note that quinine causes splenic contraction. The soft, enlarging, and congested spleen of acute and subacute malaria can alone undergo contraction. Thus blackwater fever does not usually occur in cases of chronic malaria with large fibrous non-contractile spleens. The action of other antimalarial drugs in causing splenic contraction has apparently not been described.

It may be added that Butts (1945) thinks that the sensitizing agent in malaria parasites is an Rh-like substance. Iso-immunization against it causes haemolysis in blackwater fever.

3. *Blackwater fever is the result of imbalance between lytic agents and their inhibitors. Antimalarial drugs inactivate inhibitors.*—Lytic agents in tissues have been reported by Maegraith, Martin, and Findlay (1943), Ponder (1944), Brown and his colleagues (1944), and Brückmann and Wertheimer (1945), and in the blood by Laser and Freidmann (1945). Maegraith and his colleagues suggest that the natural haemolysis which occurs normally in the body depends on the balance between the lytic agents and their inhibitors. They found that sera of blackwater fever cases during a haemolytic crisis and the sera of cases of acute malaria were less potent in their content of inhibitors than the sera of normal persons. It seems that in blackwater fever the precipitating factors directly or indirectly bring about a reduction or absence of the inhibitors.

Laser and Freidmann (1945) isolated a haemolytic substance from normal human plasma. More recently Laser (1948) has found the same substance in much higher concentrations in the blood of monkeys heavily parasitized with *Plasmodium knowlesi*. The parasites seem to produce it or cause its appearance in the infected cells, which are destroyed when its concentration is high, and the substance is thus released into the plasma to increase the concentration of lytic agents.

Nocht and Kikuth (1929) found that haemolytic amboceptors produced in rabbits by the injection of dog's blood have an increased haemolytic effect *in vivo* but not *in vitro* if quinine is simultaneously or subsequently injected. It was found that small amounts of haemolytic amboceptors—not enough to produce even haemoglobinaemia—produced haemoglobinuria when given with quinine. It therefore seems that quinine is capable of suspending or at least considerably weakening the neutralizing effect of inhibitors *in vivo*.

4. *Blackwater fever is caused by acidosis. Acid salts of quinine especially predispose.*—Any suggestion that acidosis may play a part in haemolysis *in vivo* in blackwater fever is difficult to contemplate, as acidosis associated with changes in the *p*H of blood is incompatible with life. Acid salts of quinine, however, especially seem to predispose to blackwater fever. *In vitro*, sodium bicarbonate inhibits haemolysis by antimalarial drugs.

5. *Antimalarial drugs directly aid haemolysis in blackwater fever.*—Zylmann (1944) found that a solution of quinine had a haemolytic effect on red blood cells from a normal as well as from a malarial subject, but mepacrine acted more vigorously on cells from the latter. Birnbaum and his colleagues (1945) found that, *in vitro*, quinine was haemolytic in a dilution of 1 in 200. When quinine, mepacrine, or pamaquin was not haemolytic in a given concentration, addition of bile salts precipitated haemolysis, but

sodium bicarbonate exerted a delaying effect. Singh and Singh (1944) found that quinine 1 in 300, pamaquin 1 in 10,000, and mepacrine 1 in 500 accentuated the haemolysis caused by serum obtained from blackwater fever cases.

In vivo, Ross (1927) found that malarial patients treated with quinine or pamaquin show initially an increased bilirubinaemia. It is highest about the first day and takes a few days to return to normal. Hughes and Shrivastava (1930) noticed a similar effect within twenty minutes of an intravenous injection of quinine.

Antimalarial drugs may therefore directly aid the haemoclastic crisis in blackwater fever.

Use of Antivenene.—Antivenene apparently helps in controlling haemolysis in blackwater fever (Singh and Singh, 1944, 1945, 1946; Tandan, personal communication). High doses prevent a second attack, and with smaller doses the haemolysis can be milder. Along with its use, mepacrine and quinine, even in full doses, were found to be safe in treating the residual malaria when necessary. Ponder's (1944) finding that the inhibitors present in tissues were not species-specific offers a probable explanation of the beneficial effect of antivenene. Its use supplies non-specific inhibitors. The dose of antivenene required would apparently depend on the balance between concentration of haemolysins and their inhibitors in the blood. Judging from clinical results and from the analogy of the action of antidiphtheritic serum, it is probable that the concentration of antivenene falls to 50% of the original in three to four days and gradually to zero in 10 to 14 days.

Summary

Two cases of blackwater fever due to proguanil are described. The role of antimalarial drugs in precipitating haemolysis and the role of antivenene in its prevention are discussed.

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A description of the Singapore Medical Plan is given in the recently published "Annual Report of the Medical Department of the Colony of Singapore" for the year 1951. The plan envisages the modernization and enlargement of all the existing hospitals, the building of a new hospital centre, the expansion of the Tan Tock Seng Hospital to an 800-bed tuberculosis centre, a modern settlement for lepers, improved facilities for the treatment of mental diseases and mental deficiency, a chain of maternity and child welfare clinics throughout rural Singapore, a modern quarantine station, and an improved school medical and dental service. The report states that the plan seeks to double the present facilities in all medical fields, and "will take us quite a long way on that road to a free service for all, so ardently desired by so many of the community."

RENAL EXCRETION OF UREA IN THE WEST AFRICAN

BY

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During the course of a metabolic investigation on apparently healthy male West Africans low rates of urea elimination were consistently encountered despite the fact that the subjects were living on an *ad lib* self-selected diet apparently adequate in protein (about 70 g. a day, one-third of which was meat) and calories. It was decided, therefore, to investigate, on a somewhat larger series of subjects, the "normal" level of urea output and the output following the oral administration of urea.

Methods

Ten male West Africans, all apparently healthy and with no history of renal disease, acted as experimental subjects. Five Europeans, resident in the unit, were also investigated simultaneously with the Africans in order to provide a comparison with European figures determined under the same climatic conditions.

The subjects reported to the laboratory at 8 a.m., after their usual morning meal, and remained until the end of the investigation either sitting at rest or lying on a bed. Urine was collected hourly for three hours, during which time no fluid was taken. At the end of this period the urine flow was regularly of the order of 1 ml. a minute. It is customary in conducting urea-concentration tests in a temperate climate to withhold fluid from the subject for a period of eight to twelve hours in order to ensure a high degree of concentration of the urine (Harrison, 1937). In a tropical environment, however, a period of three hours' water deprivation seems to lead to an adequate reduction of urine volume.

At the end of this preliminary three-hour period the bladder was emptied and collections were made every hour for a further period of three hours. At the end of the first hour 20 g. of urea dissolved in 100 ml. of water flavoured with orange squash was administered by mouth. In this way a sample of the "resting" rate of excretion was obtained, together with two-hourly samples following the administration of urea on which could be estimated the maximum concentration achieved and the total excretion during the period. The urine samples were analysed for urea by the method of Karr (1924), the final colorimetric determination being performed in the Coleman junior spectrophotometer set at a wavelength of 5,000 A.

Results.—The results obtained are set out in the Table.

It will be observed that in the case of every parameter the European values are higher than those obtained on the African subjects and are in tolerable agreement with the commonly accepted "normal" values for the European investigated in a temperate climate. The differences between the mean values for the two groups are statistically significant ($P<0.01$).

Discussion

The fact that the African shows a low resting rate of urea excretion might at first examination be held to be due to a low dietary protein intake. Such data as are available, however, fail to support such a suggestion; the output of urea appears to be equally low in subjects living on a diet which they themselves have to buy and in subjects living on a diet provided by the laboratory which certainly has an adequate protein content. Even when a load of urea is presented to the kidney the African fails to excrete as much as the European; the maximum concentration achieved by the African subject is at times so low as to

Subject	Age (yrs.)	Height (cm.)	Weight (kg.)	Resting Excretion*	2-hr. Excretion†	Max. Conc.‡
European Subjects						
M.L.T. ..	42	185	72	0·595	3·316	3·110
N.A.B. ..	38	183	88	0·390	4·260	3·430
P.G.P. ..	33	173	62	0·517	3·800	2·940
W.S.S.L. ..	41	176	68	1·148	4·015	2·733
R.A.K. ..	28	183	80	0·330	3·540	3·060
Mean ..	36	180	74	0·596	3·786	3·055
s.d. ..				0·291	0·334	0·228
African Subjects						
La ..	20	160	56	0·354	2·766	2·840
Sa ..	32	171	63	0·150	1·268	1·350
Go ..	26	174	54	0·240	2·780	1·780
An ..	35	156	57	0·144	2·590	1·630
Wm ..	40	156	53	0·354	2·564	1·800
Pa ..	28	170	56	0·401	2·037	1·886
Ma ..	38	148	44	0·257	2·727	2·400
Os ..	28	178	60	0·358	2·438	2·720
Jo ..	28	150	43	0·239	3·072	1·330
Ge ..	25	167	65	0·212	1·073	0·793
Mean ..	30	163	55	0·271	2·332	1·793
s.d. ..				0·091	0·634	0·611

* Grammes of urea excreted during the hour prior to the administration of urea.
† Grammes of urea excreted during the two hours following the administration of urea.
‡ The maximum concentration of urea achieved during this two-hour period expressed as grammes of urea per 100 ml. of urine.

suggest, on normal standards, a marked degree of renal impairment. More elaborate functional tests (which will be reported in full elsewhere) have, however, failed to show any abnormality in either the glomerular filtration rate or the rate of perfusion of the kidney by plasma water.

The low normal plasma urea concentration of these subjects, which is of the order of 14 mg. per 100 ml. of plasma, has been briefly reported by Phillips and Kenney (1952). This finding, together with the low urea outputs here reported, is of interest in view of the diagnostic significance attached to these values in kwashiorkor (*British Medical Journal*, 1952). It may well be that the low levels of excretion and plasma concentration reported in this condition are, in part at least, physiological and not due to pathological processes.

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Medical Memorandum

Bronchography in Children

Bronchography in children is, in general, not a simple procedure, and numerous attempts have been made to simplify the technique. Puncture of the cricothyroid membrane, intubation and injection of the iodized oil down a catheter introduced into the tube, or direct passage of a catheter into the larynx through the mouth or nose, all have the disadvantage of reducing the lumen of the larynx and interfering with adequate oxygenation.

Temple and Gray (1950) have evolved a very simple technique. They pour 20 ml. of lipiodol over the back of the tongue of the previously anaesthetized child; this method certainly has the advantage of simplicity. In the past 18 months we have obtained very good results by injecting the required amount of oil from a 10-ml. syringe into a Phillips airway placed in the mouth. If the airway is lifted forwards the distal end compresses the base of the tongue and points directly towards the larynx. This is merely an extension of the method whereby the oil is injected into the larynx, over the base of the tongue, from a syringe attached to a curved cannula, except that the airway replaces the cannula.

The technique should meet the following requirements: (1) it should be as simple as possible; (2) it should be as speedy as possible; (3) no inflammable agent should be used in the *x*-ray room; (4) the cough reflex should be abolished; (5) return of consciousness and the cough reflex should be rapid; and (6) the minimum quantity of lipiodol should be used. Adequate postural drainage of the affected lobes for 10 to 14 days before the examination is first carried out by a trained physiotherapist, either as an out-patient or as an in-patient.

METHOD

The child, having been tested for iodine sensitivity, is premedicated with quinalbarbitone sodium ("seconal") and atropine according to age, and is induced with nitrous oxide and oxygen, a flow of 2 litres per minute of oxygen and 4–6 litres per minute of nitrous oxide being eventually reached. Chloroform is added from the machine until stage 3 plane one (lower half) is reached, when carbon dioxide 1 litre per minute is added for a few breaths. The mask is removed and a Phillips airway inserted and tilted upwards so that its distal end compresses the base of the tongue and thus points towards the larynx. For a child of 5, 5 ml. (or more, according to age) of lipiodol is injected down the airway direct from a 10-ml. syringe. This is enough to fill the bronchial tree of one lung. The oil can be heard entering the larynx, as a gurgling sound is produced during respiration. The mask is reapplied, only nitrous oxide and oxygen being given, and the child is then turned quickly on to the side to be filled. Usually, no further posturing is required, but better filling of the anterior basic branches of the lower lobe can be obtained by sitting the child up and leaning him forward towards the appropriate side. Films are then taken, and while these are being developed the procedure is repeated if the bronchi on the other side are to be outlined. The amount of chloroform is minimal, averaging 1 drachm (3.5 ml.). The child is kept anaesthetized with nitrous oxide and oxygen only, until the films are developed; if these are satisfactory he can be allowed to regain consciousness. Screening can also be performed, but this is not essential.

Immediately after the operation the child is tilted into the head-down position, and each lung is then percussed and drained for about two to three minutes. In this way most of the injected oil is recovered. This is an important part of the technique. The total duration of the procedure is usually in the region of 15 minutes, and by the time the child leaves the *x*-ray department he is invariably a good colour and the reflexes have returned.

RESULTS

This technique has given very satisfactory results in our hands; any non-inflammable anaesthetic agent may be employed, but our preference for choloroform is determined by its freedom from the spasm associated with thiopentone, and the depth of anaesthesia is greater than that obtained with trichlorethylene.

The children are a good colour on return to the ward, and oxygen is very rarely required post-operatively; they are generally sitting up and taking an interest in their surroundings in one and a half to two hours after the bronchogram. It is of considerable importance that the follow-up radiographs show that the oil has almost completely disappeared from the lung fields in two to three weeks, and this is a great advantage if further bronchograms are required within a short period.

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Reviews

FORENSIC MEDICINE

Modern Trends in Forensic Medicine. Edited by Keith Simpson, M.D.(Path.), London. (Pp. 327; illustrated, £3.) London: Butterworth and Co. 1953.

Those engaged in medico-legal work will welcome this book, which consists of a series of articles by 10 specialists on different subjects of medico-legal interest. Dr. Simpson, its editor, has himself contributed chapters on the more general aspects of the subject. Perusal of the list of contributors indicates the highly varied work of those undertaking medico-legal practice and the difficulty confronting a reviewer.

The individual articles are unrelated, and, though each has its own value, they are not of equal importance in practice. The first two chapters are on the conditions relating to stillbirth and neonatal death, and are on the whole satisfactory. The difficulty of establishing the fact of live birth even after full necropsy and microscopical examination is fully discussed and possibly overemphasized. Not everyone will agree that the vernix membrane always contains stainable fat, and errors may be made if it is thought that the presence of fat is essential for its identification. The difficulty of distinguishing between a lung expanded by inhaled liquor amnii and one expanded by air has been rather overdone, and there are one or two other points that are debatable—for example, whether any baby ever died of uraemia two hours after birth, and whether anyone accustomed to doing necropsies on children could miss meconium ileus.

The chapter on the estimation of the time since death is of great interest. Further work along these lines is indicated, for if any one of the estimations is examined it will be observed that the difference in range on either side of the mean is too great to warrant a precise opinion in a court of law. There is an excellent review of physical aids in criminal science, in which the importance of microscopy, spectroscopy, photography, and radiology in medico-legal work is adequately stressed. The chapter on blood grouping is full and informative, and the article on sexing and reconstruction of the skeleton is very good. Chapter 9 is an effective discussion of the value of electro-encephalography: it is a well-informed, critical, and reasonable review, which will be of great interest to medical practitioners. The author of this chapter is commendably restrained throughout, and his contribution indicates many avenues for further investigation.

The book is readable, clearly printed, and well illustrated, and it will act as a stimulating agent in medico-legal circles. It is not suitable for the student, but should find its place on the bookshelves of all those in medico-legal practice.

SYDNEY SMITH.

THE AUTONOMIC NERVOUS SYSTEM

Anatomy of the Autonomic Nervous System. By Professor G. A. G. Mitchell. (Pp. 356; 131 illustrations, many in colour. 55s.) Edinburgh and London: E. and S. Livingstone. 1953.

Professor Mitchell has made an intensive study of the peripheral ramifications of the autonomic nervous system over a period of nearly 20 years. The careful dissections he made during this time form the nucleus of this book. Its scope is mainly restricted to an account of the peripheral pathways and central connexions of the autonomic system; it contains little information derived from experimental work and comparative anatomical studies.

The book opens with a brief historical survey, followed by an account of the development of both the central and peripheral components of the autonomic system. Unfortunately the author does not extend his historical survey later than the work of Langley. The chapter on the histological appearances of the ganglion cells and their terminal ramifications among smooth muscle and glandular cells is too short to give an adequate account of these intricate structures. The extensive literature on the vexed question of the mode of termination of postganglionic nerve fibres is reviewed rather briefly, and the only reference to the much-debated problem of the possible autonomic innervation of striated muscle is a mention of the work of Boeke (1913). No reference is made to the fact that several later workers have disputed Boeke's contention that striated muscle is autonomically innervated.

The section of the book on the central connexions of the autonomic system is particularly good and contains a comprehensive and up-to-date review of the literature. The final section, on the autonomic innervation of the viscera and limbs, will receive enthusiastic welcome from anatomists and surgeons. The illustrations are beautifully reproduced, and the intermixture of accurate drawings of dissections with actual photographs should make it simple for the reader to follow the text descriptions. The author departs from generally accepted teaching by including the olfactory (first) and spinal accessory (eleventh) cranial nerves in his classification of autonomic nerves. The reasons for doing so, especially in the case of the spinal accessory, are not convincing.

The general quality of the production is first-class, and there is a good index.

D. H. L. EVANS.

PAIN RELIEF IN CHILDBIRTH

Relief of Pain in Childbirth: A Handbook for the General Practitioner. By W. C. W. Nixon, M.D., F.R.C.S., F.R.C.O.G., and Shila G. Ransom, M.R.C.S., D.A. (Pp. 109; illustrated. 7s. 6d.) London: Cassell and Co. 1951.

This is a short and excellent account of anaesthetic and analgesic methods in obstetrics; it is primarily intended for the general practitioner and midwife. Short as it is, a surprising amount of information is contained in the 100 pages; and in each of the seven chapters there are statements of fact, or expressions of opinion, which even the specialist worker will read with interest and profit. The book is up to date, and material from almost every worthwhile paper of recent years seems to have been included.

The authors consider all forms of pain relief. There are sections on hypnotism and relaxation exercises, the sedative drugs, gas–air and gas–oxygen machines, volatile anaesthetics, local analgesics, and caudal and spinal analgesia. The apparatus required, and the practical points in the technique of administration, are fully discussed. Subjects such as the antenatal preparation of the patient and resuscitation of the newborn baby are included.

As is to be expected from the authors, both theoretical and practical sides receive full attention. For example, they give an interesting description of certain aspects of the physiology of respiration in the newborn (incidentally, the use of lobeline as a stimulant is damned with faint praise); while on the practical side they fully discuss the place of spinal analgesia and the technique of its administration for forceps delivery and for caesarean section. The style of writing is clear, and illustrations are included wherever necessary. This book can be strongly recommended to all who minister to women in labour.

J. CHASSAR MOIR.

SPEECH THERAPY

Residential Speech Therapy. Edited by C. Worster-Drought, M.D., F.R.C.P., F.C.S.T. A Record of the Work in Speech Therapy and Education at Moor House School. (Pp. 150; illustrated. 15s.) London: William Heinemann Medical Books. 1952.

This little book describes the work of Moor House School during the first two years of its existence. There are nine contributors, including the editor, whose introduction is interesting, comprehensive, yet concise. Before Moor House School was opened it was decided that facilities should be

given for the further investigation of cases of "congenital auditory imperception," which includes congenital word and language deafness. This term was suggested by Worster-Drought and I. M. Allen. Other cases are now taken, since C.A.I. would appear to be very rare.

The close attachment of the West End Hospital for Nervous Diseases to Moor House is of the greatest value, for special tests such as electroencephalography can be carried out. There is an interesting comparison between the merits of out-patient treatment and those of treatment given in a residential school. At present Moor House is the only school of its kind in the country; cases have been received from only 46 local education authorities, but doubtless when the school is better known there will be many more applications for entrance. It may be wondered whether an I.Q. of 80 is not rather on the high side as a minimum standard for admission. The future policy of the school is to continue to investigate and treat all possible cases of aphasia, both executive and receptive. A scheme is being considered of treating in a special class cases of alexia or dyslexia, which might be termed congenital visual imperception; the out-patient treatment of these cases has not proved satisfactory.

Appendix A is most instructive on the detailed account and treatment of five cases. Here the guidance of Dr. W. F. Coningsby has been used. Appendix D gives the sound-alphabet, with pictures compiled by Dr. Coningsby. It is very interesting, but it is a pity that the usually accepted triple rhythm is not adhered to in every example. The illustrations are good and the book is well set out, but a bibliography might have been helpful. The work of Moor House School deserves every encouragement, and it is to be hoped that it will extend its field of research to all branches of speech therapy.

E. J. BOOME.

GENETIC RESEARCH IN GENERAL PRACTICE

The Treasury of Human Inheritance. Volume V. *On Hereditary Digital Anomalies.* Part 1. *On Brachydactyly and Symphalangism.* By Julia Bell, M.A., F.R.C.P. (Pp. 31; 19 figures; 10 pedigree plates. 12s. 6d.) London: Cambridge University Press. 1951.

With a new volume of this fine series Dr. Julia Bell has turned from neurology to skeletal abnormalities, a field in which careful reviews of the literature, with a clear classification of types of anomaly, should prove equally rewarding. Her definitions have been widely drawn, and she recognizes eight groups and subgroups, which show relatively little genetic overlapping. As with so many skeletal defects, all behave as dominants, though there are certain curious anomalies. There is an interesting discussion of the severe dwarfing which may occur in the classical form of brachydactyly—a dwarfing which seems to be unlike any other. The admirable standards of production of the earlier volumes are maintained, as is the modest price.

Quite the most remarkable feature of this number, however, is the extent to which it is based on the work of a physician who died in 1925 at the age of 70, having spent his life in general practice; indeed, it might well have been called the Harry Drinkwater Memorial Number. Apart from numerous references, no fewer than 16 out of 19 illustrations are his. That even to-day a monograph must necessarily quote him so extensively should be an encouragement to those who hope that there is still opportunity in genetic research for the clinical observer, and who regret the fact that the Nettleships, the Ushers, and the Drinkwaters have so few successors in the present generation. Incidentally, Dr. Bell does less than justice to one, and only one, of his observations: the well-known story of symphalangism in the first Earl of Shrewsbury and in some of his remote descendants. She merely remarks in the note on the pedigree: "There was a tradition in the family that an ancestor who died in 1453 had presented the same anomaly." Drinkwater's own account (*Proc. roy. Soc. Med.*, 1917, **10**, Sect. Path. 60) is detailed and specific. After describing how the skeleton of John Talbot came to be examined in 1874, he says: "Bishop Abraham (assistant bishop of Lichfield) visited Whitchurch at this time and was shown the bones by the Rector, the Rev. W. H. Egerton. . . . Bishop Abraham was a very intimate friend of A.T., and knowing of his digital peculiarity at once examined the bones of the fingers, and discovered the same ankylosis that exists in the fingers of A.T., and he wrote to his friend to inform him of what he had found. An account of these bones was written by Mr. Egerton, the Rector, and published in the Standard in 1877."

J. A. FRASER ROBERTS.

INDUSTRIAL DERMATOSES

Dermatoses Professionnelles. By Professor H. Gougerot and A. Carteaud. (Pp. 370; 61 figures. 2,000 francs.) Paris: Librairie Maloine. 1952.

This excellent survey of occupational dermatoses is clearly laid out, comprehensive, and well balanced. The book is divided into four sections. The first is on the various dermatological conditions which may arise from occupational causes, and the authors discuss their diagnosis, pathogenesis, and treatment. In the second they consider systematically a large range of occupations and describe the various dermatoses to which they may give rise; the conditions vary from bee stings in apiarists to lipstick dermatitis in cinema artists and scurvy in Arctic explorers. The third part is a tabulated list of potential cutaneous irritants, and the fourth is on the compensation aspects of cutaneous dermatoses according to French law.

The book contains a vast store of useful information; it is interesting to learn, for instance, that even handling gold may produce dermatitis. But one cannot always agree with the authors' theoretical conclusions as exemplified by such statements as, "The eczema burns the toxins, hence the redness, heat, and pain," and, "A healthy skin will not let itself be impregnated by an irritant placed on it." There is a good account of barrier creams and also of patch tests, of which they describe three types—on skin from which the grease has been removed by ether, on skin lightly rubbed with emery paper, and on scarified skin. Preventive measures for dermatitis are well discussed, and the authors suggest that desensitization should always be tried; in our experience this is rarely if ever successful. There is no very clear statement about "hardening," which Schwartz considers such an important defence against dermatitis, and prognosis is hardly touched on, probably because there is so little accurate information about it in the world literature. There are many rather dark black-and-white pictures. These are the least satisfactory feature of a book which we can otherwise thoroughly recommend to all dermatologists and industrial medical officers.

F. F. HELLIER.

All those who play ball games—or play at them—will know the exquisite thrill of the perfect shot. The pleasure lies not so much in the consequent success as in the perfection of balance and co-ordination of muscular movement which make up the physical performance. How to attain perfection is the problem of all players of games in which the movements are of a swiftness which veils their nature. The spate of books, on golf in particular, is proof of the essential difficulty of the subject. The "rabbit" and the professional alike are equally frustrated when they try to analyse for the benefit of others the mechanics of the perfect swing. If capable of telling us, could a duckling describe how it takes to water? Dr. H. A. Murray in his book *The Golf Secret* (6s.; Kingswood, Surrey: Elliott's Right Way Books) has got very near to giving what he claims to give—the key to the "golf secret." He writes clearly and didactically, and his "secret" is eminently simple in fact and exposition. Moreover, he does not command each part of our anatomy in turn until we feel like a gawky schoolgirl or the poser for a photograph, but the mechanics of his theory (illustrated by excellent diagrams) are based on simple anatomical facts. He may well be right. If he is, then this book will remove some of the hazards of what is a secondary occupation with so many medical men.

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SICKNESS ABSENCE IN INDUSTRY

The illnesses which keep men from their work have long been a matter of concern to industrialists and administrators, for they lead to much loss of time and interfere seriously with production and efficient administration. The latest report of the Ministry of National Insurance[1] shows that in Great Britain on an average day in 1950 no fewer than 908,000 people were drawing insurance for sickness absence. This does not include absence from industrial accidents nor from prescribed industrial diseases, nor all the trivial but common absences lasting less than four days. Even so it represents 1 in every 25, or 4% of the insured population. It is natural to wonder what, if anything, can be done to reduce this toll of ill-health. The second world war and the subsequent economic difficulties of our country have given a particular emphasis to this long-standing problem, and it has been studied by a number of investigators in recent years.

The first need is for adequate records. Although every business concern must keep some records for its pay department, these may not be suitable for further study; in particular, they may be defective as records of the medical causes of absence. Hughes[2] has recently outlined a system which should find wide acceptance in industry. He has drawn on a previous report[3] from the Medical Research Council and also on the experience of the London Transport Executive, which uses an exceptionally comprehensive and detailed system,[4 5] and he makes some eminently practical proposals. They are intended as a guide for factories with 50 to 1,000 employees: smaller factories hardly need any detailed system and larger ones probably have their own already. Hughes outlines suitable methods for keeping a register of persons absent through sickness or accident, and for transferring the information to record cards for each individual, from which suggested analyses may be made. The diagnosis recorded is that on the statutory medical certificate. This is more reliable than many of its critics allow. Raffle[6] and a colleague, making routine examinations of 3,500 London Transport employees on their return to work after sickness, found that 55% of their diagnoses fell into the same 3-figure code of the 1948 International Statistical Classification of Diseases as that on the medical certificate. When the diagnoses were grouped into 21 broad categories, the extent of the agreement rose to 80%. Hughes recommends the same classification for the diagnoses, but condenses it into twelve broad groups for the smaller factory.

But the system of recording is only the means to an end, and it would be well to consider how useful such sickness records may be. The conclusions that can be reached from statistical analyses of such data are well illustrated by Roberts[7] and by two papers from the Oxford Institute of Social Medicine.[8 9] Older employees are absent more often, and lose more time, than younger employees, and the rates are higher for women than for men. The nature of the work influences absence rates, but in analysing such rates it is difficult to separate the effects on them of the arduousness of a job from those due to the attraction the job may have for men of particular physique or state of health. Such surveys can also indicate the relative importance of different diseases as causes of absence and of lost time. The direct studies of insurance medical certificates which were made by the Department of Health for Scotland[10] before the second world war are particularly informative here. But many other influences can affect the level of sickness absence of a group of workers. Roberts states that "psychological factors influencing sickness perhaps outweigh all others," and cites evidence that the quality of supervision of a group of employees can have a considerable effect on their liability to be absent through sickness. Economic factors are also important, as is clearly demonstrated in two recent papers about the effect of sick-pay on sickness absence. One, a most elegant study by Denerley,[11] contains an analysis of sickness absence among the 40,000 employees of a large industrial organization before and after the introduction of a system of paid sick-leave. For the twelve months before the change their level of sickness absence was the same as that of 41,000 non-established workers with no paid sick-leave in a second large industrial organization. The effect of the new system was

1 *Second Report of the Ministry of National Insurance for the period 5th July, 1949, to 31st December, 1950.* London: H.M.S.O. 1951.
2 *Brit. J. industr. Med.*, 1952, **9**, 264.
3 *Rep. industr. Hlth Res. Bd*, London, No. 85. 1944.
4 Spratling, F. H., and Lloyd, F. J., *J. Inst. Actuaries*, 1951, **77**, 196.
5 Raffle, P. A. B., *Trans. Ass. industr. med. Offrs*, 1951, **1**, 72.
6 Ibid., 1951, **1**, 87.
7 Ibid., 1951, **1**, 65.
8 Russell, W. T., Whitwell, G. P. B., and Ryle, J. A., *Brit. J. industr. Med.*, 1947, **4**, 56.
9 Sutherland, I., and Whitwell, G. P. B., ibid., 1948, **5**, 77.
10 *Reports on Incapacitating Sickness Among the Insured Population of Scotland*, 1931–7. (A series of seven.) Edinburgh: H.M.S.O. 1932–8.
11 *Brit. J. industr. Med.*, 1952, **9**, 275.
12 Ibid., 1952, **9**, 282.

simple and dramatic. The percentage of working shifts lost from sickness doubled within three months, and thereafter the level of absence was identical with that among the 20,000 established workers in the second organization who had long been entitled to paid sick-leave. Buzzard and Shaw[12] show a similar rise in sickness absence after the introduction of a sick-pay scheme among 8,000 industrial workers in Government employment.

The conclusion to be drawn from these studies is not the obvious one—that an important way of reducing sickness absence would be to stop existing schemes of sick-pay. It would be misleading to attribute all, or even much, of the extra absence to malingering. The loss of earnings entailed may have kept many men at work before the change who should have been in bed, and may have discouraged many more from even a brief convalescence. When the financial stringency is removed, such men can afford to get really well, and they may return to work not merely better physically and mentally but less likely to become seriously ill in the future. To abolish schemes of sick-pay would almost certainly reduce the amount of absence, but it would not increase the health of the worker nor, in the long run, his productivity. It seems therefore that, although a man's absence from work on account of sickness, and also its duration, are real manifestations of ill-health, they are also affected by complex outside influences, many of which are either immeasurable or assessable only with difficulty. It is thus hard to reach useful conclusions from statistical analyses of sickness absence, and he would be a bold factory doctor who would attempt it from the records of 1,000 employees or even of a much larger number. Indeed, London Transport, whose bus drivers and conductors probably constitute two of the largest homogeneous occupational groups of workers in the country, has not ventured to publish more than illustrative results until it has three years' records available.

This does not mean that because it is an unsuitable basis for complicated statistical analyses a good medical record system is a waste of effort in the smaller factory. Even a simple system, if it is well kept, will improve the doctor's knowledge of each individual worker and direct his attention to parts of the factory where the prevalence of sickness is strangely high or low. Out of his detailed knowledge of the working conditions, the health, and the personalities of those in his charge, the factory doctor should gain more ideas on how to improve the health of the employees than by concentrating on absence statistics, which are only one of its manifestations.

RESEARCH IN GENERAL PRACTICE

General-practitioner research seems to be in the air this spring. The G.P. himself, often shy about his aspirations, may need encouragement and advice in overcoming the various difficulties of combining research with general practice. The first obstacle is the attitude of mind that the sick man expects in his medical attendant—assurance in diagnosis and confidence in prescribing. If he feels his doctor to be uncertain in these matters it may impair his trust and even adversely affect the course of an illness. The good general practitioner has to be dogmatic and assured even when dogmatism is not altogether warranted by the state of current knowledge. The attitude of the research worker is of course different. His ignorance must always be strongly before him, so that the unexplained facts of human illness continually abutting on his awareness clamour for an explanation. Although the two states of mind can coexist in the same individual, they make uneasy bedfellows, and the general practitioner may well find it a strain to maintain critical integrity alongside diagnostic and therapeutic dogmatism. The successful combination of the two attitudes in one doctor is therefore unlikely to be a common phenomenon, and the efforts now being made to discover the G.P. research worker, remove his difficulties, and aid his development deserve every encouragement.

A second difficulty in the way of the G.P. research worker is the necessity for uninterrupted time. Professor Robert Platt points out in the lecture published in the opening pages of this issue that good research needs careful planning. The detailed preparation of a research task is time-consuming, and the general practitioner is at a grave disadvantage because time for consecutive work occurs seldom, is not often predictable, and never dependable. Consequently it is sometimes thought desirable to limit general-practitioner research to such experimental projects as the therapeutic trial for which preparation is minimal or can be stereotyped and done by others. For example, does sulphonamide given prophylactically prevent the complications of measles ? The research-minded practitioner may plan a simple experiment to apply to his next outbreak. Professor Platt cites a number of similar problems which could usefully be settled by general practitioners working singly or in groups.

Doubtless many practitioners have pet problems which they would like to submit to investigation, and indeed general practice provides a rich field for both observation and experiment. Of the acute illnesses encountered, a precise diagnosis can be truthfully

applied to less than 20%. We are similarly in ignorance about the real nature of some common diseases universally supposed to be infectious, and for few communicable diseases can the mode of spread be described with certainty. Some general practitioners are doubtless hoping to take part in an attack on long-term problems such as these, but before the fertile ideas that may have occurred to them can come to fruition much careful thought will have to be given to appropriate methods of research. The general practitioner attempting work of this sort may spend many weary hours planning the approach to a problem and make considerable headway, only to be torn away from it for perhaps two or three weeks by unavoidable obligations. He eventually returns to it to find that his varied preoccupations have meanwhile chased the details out of his head and he must spend more hours familiarizing himself with his own proposals. When interruption occurs, as it may, again and again both in the planning and in the analysis, the appetite for research is dulled, otherwise many more general practitioners might have contributed valuable information to the fundamentals of medicine. Encouragement like that given by Professor Platt, especially when combined with excellent practical advice, is both needed and welcome.

Most scientists have secretarial help and access to libraries, laboratories, university departments, or industrial organizations. These contacts keep them in touch with work in their own field and in those fields which border it. They can spend weeks or months studying the technique of others wherever they may work. On the other hand, the general practitioner, especially in the country, is isolated both from his colleagues and from these other sources of stimulation. His patients would not take kindly to his frequent or prolonged absence. Consequently his original contributions are apt to be jejune because he does not know how much of his ground has already been covered ; alternatively, he may refrain from publishing observations of importance because he is not in a position to recognize their value. If general-practitioner research is to bear the fruit it ought, the G.P. scientist should be afforded the opportunities which have been found valuable for research workers in other fields. Unfortunately, this simple and obvious proposition may be far from easy to implement. But in spite of the difficulties a number of general practitioners have done excellent work with no other help than that of their wives, and it is to be hoped that this fine tradition will continue. There is a danger, however, that the very successes of these pioneers may limit the vision of their successors, and of the patrons of G.P. research, to a restricted view of the scope of investigation which can be attempted in general practice with any chance of success. The Medical Research Council is taking an increasing interest in this field of study, and the College of General Practitioners is also setting up a committee to encourage general practitioners who wish to do research. Both these bodies are aware of all the difficulties, and may be able to offer practical help to any general practitioner engaged in research work or desirous of participating in it. But new knowledge is usually gained at a price, and even the wisest assistance from others may be unable to spare the conscientious research worker considerable personal sacrifice.

CAUSE AND EFFECT

The widespread use of new drugs before possible side-effects have been studied is a frightening feature of modern medicine. The review by Macht[1] of the action of drugs on blood coagulation might seem a welcome contribution to the study of an undesirable side-effect of therapeutic drugs. The thesis supported by Macht is that many drugs have a "thromboplastic" effect because they shorten the clotting time, and that since they have this effect they predispose to thrombosis. If this contention is true it is obviously important, because clinical impression suggests that the incidence of thrombosis has increased. But the evidence on which this review is based is not convincing.

The evidence that drugs affect clotting rests mainly on studies with a modification of the Lee and White clotting time. This test is notoriously difficult to use. It is influenced by many factors, such as the size and shape of the tubes used, the size of the syringe and needle, and the facility with which blood is withdrawn. The range of variation to be found in normal human subjects is large. In Macht's experiments the variation appears to be particularly large. In frightened human subjects clotting times as short as one minute are recorded. Since this figure is quite unbelievably short, it is difficult to avoid the conclusion that some technical factor must have influenced the results. In an experiment on rabbits[2] the normal clotting time varied from 6 to 23 minutes, which is a very wide range. It is true that when enormous doses of "digoxin" were given to rabbits[3] the clotting time shortened, but there is no evidence that therapeutic doses would have the same effect. It is also claimed that penicillin in very small doses enhances clotting, but this contention is not supported by a careful study of normal and haemophilic subjects by Lewis.[4] This study is dismissed as trivial by Macht. But haemophilic blood lacks intrinsic thromboplastin and is therefore particularly sensitive to additions of thromboplastic substances. If penicillin is thromboplastic its action should be demonstrated more clearly on haemophilic than on normal blood.

[1] Macht, D., *J. Amer. med. Ass.*, 1952, **148**, 265.
[2] —— *Arch. Int. Pharmacodyn.*, 1947, **74**, 399.
[3] —— ibid., 1951, **85**, 321.
[4] *Proc. Soc. exp. Biol. (N.Y.)*, 1946, **63**, 538.

Even if the contention that the drugs studied shorten the clotting time were accepted it does not follow that the drugs would predispose to thrombosis. The whole-blood clotting time is not only an unreliable test technically, but it is also a doubtful guide to clotting efficiency. The clotting time of haemophilic blood may be restored to normal when the patient has been transfused, and yet the patient may continue to bleed. In patients who have developed thrombosis there is no reliable evidence that the clotting time is shortened, and there is much evidence that intravenous injections of thromboplastin would be likely to lengthen rather than to shorten the clotting time. Macht appears to be unaware of this difficulty in interpretation. In 1947 he wrote: "More recently certain widely employed mercurial diuretics have also been found to produce such a thromboplastic effect leading occasionally to fatal thrombotic accidents." From the work to which this passage refers this statement rests on the evidence that patients sometimes die suddenly after receiving mercurial diuretics and that these drugs may shorten the clotting time.

Conclusions based on such unreliable evidence should not deter discerning clinicians from using valuable drugs. Macht uses a quotation from the work of Ochsner, de Bakey, and de Camp to support his thesis, but it is difficult to think that these authors meant more than to suggest that the role of penicillin in the causation of thrombosis might be worthy of study.

HANDWRITING AND PERSONALITY

The complexity of the problem, and the importance attending even partial solutions, both contribute to the interest shown everywhere in attempts to measure the main dimensions of personality. One of the oldest methods of personality assessment, the study of handwriting, was thrown out of the door by tough-minded experimental psychologists in the early years of the century; it is attempting to climb in again through the window under the novel guise of a "projective" method, akin to the Rorschach ink blot or the Murray thematic apperception test. A congress held in New York in May last year[1] and a new book published in the American Lecture series[2] attest to the renewed vigour with which the ancient paths are being rediscovered. Can it be said also that the ancient fallacies are being avoided?

The weakness of graphology has always lain in the lack of validation of the claims made for it. The fundamental hypothesis that personality may influence or even determine style of movement, and that consequently the permanent record of such movement embodied in writing may be useful in giving clues to personality, is almost certainly correct. There is much empirical evidence to show that "expressive movements" of one kind or another can be used with success in psychiatric diagnosis and psychological assessment. The difficulty lies almost entirely in discovering a method which would enable us to argue backward from script or movement to personality. Graphologists are split into two camps—those who make use of certain isolated signs (such as the length of the stroke crossing the "t," or the variability of the pressure with which the pen is applied) and those who attempt to see each "sign" in the light of the total picture presented by the script. The claims of the former group are more easily tested, and much research has shown them to be almost entirely unfounded. The latter group's claims are more difficult to subject to exact experimental scrutiny, and a valid appraisal is therefore made difficult.

Several attempts have been made to assess graphologists' claims by testing not so much the method but rather the graphologist. This appears reasonable; if the graphologist himself (or more frequently herself) cannot arrive at the correct description of personality through the use of his method it is unlikely that anyone else could. Results have not been altogether unfavourable; in a number of cases the graphologist has produced agreement with the results of tests based on other psychological criteria to an extent well beyond what could have been expected on the basis of chance alone.

This of course does not justify the enthusiastic language of one graphologist at the New York meeting who claimed that graphology "has scientific value by far exceeding the bounds of what can possibly be established by any kind of quantitative investigation." Nor does it justify the practical use of handwriting analysis; nothing but harm can come from the premature application of any method to measure personality. Graphology is still in the experimental phase, and orthodox psychology may with advantage devote some time to investigating the ramifications of "expressive movements" and their relations to personality. Until the theoretical problems connected with this are solved, books claiming that "basic graphology may easily be learned by anyone" will serve only to antagonize those who approach the subject with an open but critical mind.

BRAIN METABOLISM

Mental efficiency depends ultimately on the biochemical processes going on in the brain. We are reminded of this by the usual experience of climbers who get within a few hundred feet of the summit of Mount Everest. They find that their problem is not just one of physical endurance but also of keeping their heads in the rarefied atmosphere, discounting the deceptive feeling of euphoria, and turning back from their objective in time. That mental symptoms can be caused by mild anoxia was noted early in the century by the physiologists Douglas, Haldane, Henderson, and others, who carried out their studies on Pike's Peak. It is recorded that the irrational behaviour of the visitors

[1] *New York Times* (International Edition Supplement), May 20, 1952.
[2] Victor, F., *Handwriting—A Personality Projection*, 1952, Oxford.

there necessitated the appointment of an extra deputy-sheriff. "Perhaps unreasonable people met with under ordinary circumstances are really suffering from want of oxygen," Bayliss remarked.

The first step in studying the relation of mental symptoms to brain metabolism was clearly to get some method of measuring directly the metabolic activity of the brain; but this proved difficult. The development of a technique for internal jugular puncture made it possible to determine the oxygen taken up from the arterial blood traversing the brain, but it was necessary to measure also the rate of blood flow before the metabolic activity of the brain could be known. Earlier figures for the blood flow through the brain ranged from 325 ml. per minute, obtained by the method of occluding the venous return from the internal jugular veins,[1] to 1,000 ml. per minute, which was calculated for man on the basis of measurements made on the dog.[2] More recent values from three different laboratories fall between these limits and come close to 725 ml. per minute, which can now be accepted as a reasonably reliable estimate.[3-5]

Figures for the brain metabolism *in vivo* have now been obtained for a number of conditions by Kety and his collaborators,[6] using the nitrous oxide method for determining the rate of blood flow. The cerebral blood flow fluctuates to some extent with the blood pressure and with the oxygen saturation of the blood, but the cerebral oxygen consumption normally remains fairly constant at the high level of about 3.3 ml. O_2 per 100 g. brain per minute.

In patients with cerebral tumours the brain metabolism is little affected until the intracranial pressure reaches about 400 mm. of water: there is then a consistent fall in the cerebral blood flow, associated with a diminished cerebral oxygen consumption and the onset of severe mental symptoms, usually coma.[6] Diabetic coma and insulin coma are again associated with a significant fall in the cerebral oxygen consumption, which is the probable cause of the mental symptoms in these conditions. Patients suffering from schizophrenia gave normal values for the blood flow and oxygen consumption, but patients with arteriosclerotic and senile psychoses showed a significantly lower blood flow and cerebral oxygen consumption than was found in healthy young men. The cerebral oxygen consumption is depressed by about 40% in anaesthesia and increased by up to 50% in states of anxiety and emotional excitement. The work of Kety and his collaborators has provided a store of information about the cerebral blood flow, vascular resistance, and oxygen consumption in a variety of conditions and given a valuable new approach to the study of the mental symptoms associated with metabolic disturbances in psychiatric and other forms of disease.

[1] Ferris, E. B., *Arch. Neurol. Psychiat. (Chicago)*, 1941, **46**, 377.
[2] Schneider, F., and Schneider, D., *Arch. exp. Path. Pharmak.*, 1934, **176**, 606.
[3] Kety, S. S., and Schmidt, C. F., *J. clin. Invest.*, 1948, **27**, 476, 484.
[4] Gibbs, F. A., Maxwell, H., and Gibbs, E. L., *Arch. Neurol. Psychiat. (Chicago)*, 1947, **102**, 184.
[5] Himwich, H. E., Homburger, E., Maresca, R., and Himwich, H. E., *Amer. J. Psychiat.*, 1947, **103**, 689.
[6] Kety, S. S., Shenkin, H. A., and Schmidt, C. F., *J. clin. Invest.*, 1948, **27**, 493.

PARABIOSIS

We are all familiar with the existence of Siamese twins, and some of us with their analogue in cattle—freemartins—but we are not all aware of the name that has been coined to describe the condition—"parabiosis." Finerty[1] has recently drawn attention to the manner in which a freak of nature has been imitated and exploited by the experimental physiologist. The technique derives from the early experiments of Paul Bert, who worked in Claude Bernard's laboratory. As practised to-day, the procedure consists in (*a*) a longitudinal incision of the skin from ear to base of tail on the right side of one rat and the left of the other; (*b*) union of the ventral edges; (*c*) incision of the abdominal wall from last rib to ileum; (*d*) union of the four edges of the abdominal wall; (*e*) tying the lateral aspects of the adjacent scapulae; (*f*) union of the dorsal edges of the skin incisions. Experiments with radioactive tracers have put beyond all doubt the development of direct capillary anastomoses in the parabionts, leading to an exchange of blood equal to about 10 times the blood volume per day. The existence of a so-called "parabiontic barrier," comparable with the blood–brain barrier, seemed to have been proved by the observation that certain substances passed from one parabiont to the other with great difficulty. Such a conception, however, is difficult to reconcile with the existence of a common circulation, and it was later shown that the substances were indeed passing from the injected animal to the other, but were being destroyed or eliminated too rapidly to be detected in the blood.

It was the pregnancy of one of the famous Bohemian sisters, Rosa and Josepha Blazek, that lent support to the theory that lactation was governed by a humoral mechanism. Thus, after the birth, lactation occurred in both sisters; and from this observation the value of parabiosis as an experimental technique is clear. For example, the study of pituitary–gonad interrelationships has been especially facilitated: the main basis for these studies was the observation of a striking increase in the size of the ovaries of an intact female united to a castrated male. When it was discovered that the anterior hypophysis regulated gonadal development, it was not difficult to show that the castrated male was liberating large amounts of gonadotrophic hormone and thus influencing the intact partner.

While aiding in the elucidation of many other problems involving humoral agencies—pituitary growth hormone, diabetes mellitus, renal hypertension, for instance—the technique has produced problems of its own, outstanding among which is the phenomenon of "parabiosis intoxication." This seems to be a manifestation of incompatibility between parabionts expressing itself as an anaphylactic reaction, and is thus similar to the unsuccessful "take" of a homograft. One partner, in these cases, becomes hyperaemic, and a day or so later the other shows a marked shrinkage in size, becomes anaemic, and is the first to die. Various explanations have been put forward to explain the symptoms of the dying parabiont. In general, it would seem that the

[1] *Physiol. Rev.*, 1952, **32**, 277.

intoxication is fundamentally a result of constitutional incompatibility, but the manifestations are complicated by infection, inanition, and other factors which may obscure the primary symptoms. As a tool in the study of hormonal influences, the technique of parabiosis has justified itself; as our knowledge of the chemistry of these hormones, and our skill in preparing them, increase, it becomes simpler to study their effects on a single animal, the more so since the frequency of unsuccessful takes may be as high as 64%.

IMMATURITY AND MENTAL ILLNESS

In trying to come to terms with aspects of human personality, which in their subtlety and complexity tend to be entirely bewildering, the psychiatrist is often reduced to making use of ideas of a vague and impalpable kind. Some of these concepts, despite their vagueness, clearly correspond with something essential and real in the nature of the material. When this is the case it becomes a duty to try to reduce the vague idea to a precise form, if possible the form of a characteristic which can be measured.

So it is with the idea of immaturity. Countless clinicians have been struck by the fact that the personalities of many of their psychiatric patients show qualities which they associated rather with children or adolescents than with fully adult persons. This is, perhaps, especially so with patients suffering from hysterical illnesses; their egoism, demonstrativeness, suggestibility, and emotional lability constantly recall the child. But to some extent the same feeling is likely to be aroused by such other varied classes as anxiety neurotics, delinquents, and even schizophrenics. There are, indeed, a number of clinical observations, such as the rarity with which middle-aged hysterics are seen, which strongly suggest that delayed maturation of the personality may be a predisposing cause of mental abnormality, and that the progress of maturation, after years in which it is supposed normally to cease, may contribute to recovery from abnormality. In some psychopathological theories, such as psychoanalysis, delay in psychosexual maturation is assigned a central place in causation.

In the physiological field there are observations which lead in the same direction. The outbursts of explosive irritability of the aggressive psychopath, which bear a clinical resemblance to the temper tantrums of the child, are often associated with a disturbance of the electrical physiology of the brain, as shown by E.E.G. studies, which cannot be regarded as abnormal in itself but abnormal only for the age at which it is being shown. The concept of delayed maturation has therefore become one of great value to the clinical electroencephalographer.

An investigation of the way in which immaturity may show itself in other ways has now been reported by Lovett Doust.[1] Accepting the demonstration by Kretschmer and by Sheldon and their schools that psychiatric patients of different kinds tend to differ in physique from normal subjects, Lovett Doust inquired what part of such differences of physique might be ascribed to delayed maturation. Working with 261 healthy adult subjects and 302 psychiatric patients, he made some interesting discoveries. Not only did the patients differ from the controls but they also differed among themselves. Blue eyes, long curved lashes, pouting lips, and a soft skin were found predominantly among neurotics; wide-spaced eyes and a shallow nasal root among depressives; and ears without discrete lobulation, double-jointedness, and persistent remnants of the epicanthic fold among schizophrenics. As the author points out, maturation of the growing individual proceeds in many directions at once, and it is only natural that in some it should be delayed along some lines, in others along other lines. The problem now remains to relate the different immaturities of neurotics and those of schizophrenics, if their existence is confirmed, to their psychiatric differences. One other interesting observation also arose from the work. It was found that immaturity tended to diminish with age, both in the psychiatric and in the control series, but that the rate of diminution was not so great in the former.

An interesting field is opened for further inquiry. Speculation would obviously be premature, but it does seem possible that the correlation of anatomical findings, such as those made by Lovett Doust, with physiological ones, such as those which can be provided by the E.E.G., could lead to new ideas about causation. On the other hand, the use of physical indices to make psychiatric diagnoses, which Lovett Doust suggests, is something which can be relegated to a much more distant future.

[1] *Brit. J. soc. Med.*, 1952, **6**, 169.

CHILDREN IN HOSPITAL

Just over a year ago Professor A. Moncrieff and Miss A. M. Walton[1] described in this *Journal* a new scheme of visiting successfully tried out at the Hospital for Sick Children, Great Ormond Street. The mothers of young children being treated as in-patients were urged to come to the hospital daily between 5 and 6 p.m. and help with the care of their children during that hour: they could give them their suppers, clean teeth, read a story, or play a game—in fact do just the things they would do for their children at home. There were of course difficulties in putting the plan into operation, but mothers and the nursing staff both liked it, and, more important, the danger of young children suffering serious harm[2] from being deprived of their mothers' care was reduced.

The Central Health Services Council has now given its blessing to the daily visiting of children in hospital by their parents, and the Ministry of Health has sent out a circular letter[3] urging all hospital authorities to allow this, "with adequate safeguards against the introduction and spread of infection." It is to be hoped that the advice of the Central Health Services Council will quickly be followed by those hospitals which have not yet given daily visiting a trial. At a time when the Ministry sought for information from hospitals last year only 300 out of 1,300 hospitals which admit children were allowing daily visiting; and at 150 hospitals (only half of which were fever hospitals) the visiting of children was prohibited altogether. Such restrictions are inhumane.

[1] *British Medical Journal*, 1952, **1**, 43.
[2] Ibid., 1952, **2**, 1249.
[3] H.M.C. (53) 17.

REFRESHER COURSE FOR GENERAL PRACTITIONERS

MEDICAL ASPECTS OF AIR TRAVEL—II. MEDICAL FITNESS

BY

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Air travel by invalids has become a daily occurrence. In fact for the majority of them transportation in a modern airliner is the ideal mode of travel for long distances. Though very few are unfit for air travel, some have to be rejected in the interests of other passengers or for flight operational reasons.

Unsuitable Cases

The main types of case unsuitable for air travel in commercial passenger-carrying aircraft are: (1) those suffering from infectious diseases of any kind; (2) those liable to be affected by even a small decrease in the oxygen tension—for example, patients with serious cardiac or respiratory disease, advanced anaemia, or recently irradiated leukaemia; (3) those liable to be severely affected by airsickness and lowered atmospheric pressure—for example, some cases of pregnancy, some diabetics, and cases of active peptic ulceration; (4) acute mental patients and major epileptics; (5) those with skin diseases of a repulsive appearance; (6) those with odoriferous conditions; and (7) women beyond the eighth month of pregnancy.

The general rule is to accept every case if possible, due consideration being given to the interests of the patient and of all others concerned. This at times makes selection an arduous duty, but it is much simplified by applying the formula, "Is the patient infectious, acutely ill, or does he act, look, or smell abnormal?"

Certain cases which might be rejected for public air transport might be acceptable in a privately chartered aircraft, where there would be no offence to other passengers and where the altitude and each stage of flight could be adjusted to suit the patient's condition.

Common Medical Problems

The commoner conditions on which a medical opinion may be sought on the advisability of air travel are as follows:

Anaemia.—Patients with anaemia suffer from anoxia when flying even at an altitude of 8,000 ft. (2,400 metres), especially if their red-cell count is less than 2,500,000 per c.mm. or their haemoglobin content is below 50% (7 g. per 100 ml.). They should therefore be given a transfusion to raise the red-cell count to at least 3,000,000 per c.mm. and the haemoglobin to 60%, preferably to 80%. They should remain at rest throughout the journey and oxygen should be available.

Cardiovascular disease of marked degree is present in about three-quarters of those who are taken ill during flight. The low oxygen tension, even at altitudes between 5,000 and 8,000 ft. (1,500 and 2,400 metres), throws a serious strain on the heart. These patients should travel in a pressurized aircraft and limit their movements to the minimum; oxygen and any special drugs prescribed by their doctor should be available; and the medical department of the airline should be made aware of their condition. Patients with *angina* or *coronary occlusion* should not fly unless they have been free from symptoms for at least three, preferably six, months. Even then the altitude should be limited to 5,000 ft. (1,500 metres). A test of fitness for anginal patients is whether they can walk briskly for about half a mile (0.8 km.) without symptoms. Patients with *valvular disease* should not fly while the condition is acute, nor when it is chronic if there are signs of congestive failure or pronounced anaemia. Those with *congenital heart disease* can be accepted for flights up to 8,000 ft. (2,400 metres) altitude, in the absence of venoarterial shunt, as evidenced by cyanosis, heart block, or severe hypertension resulting from coarctation of the aorta. Those suffering from *myocardial lesions* are unacceptable if there is marked bradycardia or if they have had diphtheria within six months. Cases of *high blood pressure* can be accepted if there is no pulsus alternans, cardiac or renal asthma, frequent headache, much loss of weight, gross albuminuria, cellular casts in the urine, or optic fundus change. They should be given a sedative before flight to prevent nervous tension worsening their condition, particularly if they have not flown before.

Calculus.—Those with calculus (biliary or urinary) are acceptable, provided they are not suffering from an attack, are given hyoscine before flight to prevent airsickness, and that morphine is available on the aircraft in case of need.

Diabetes.—Only diabetics who are stabilized by diet or insulin and have no obvious cardiovascular disease are acceptable for long-distance air travel, with its rapidly changing clock times and departures at all hours of the night. They must be able to administer insulin to themselves and have their insulin, syringes, and needles (plural) with them. They must be instructed to keep strictly to the clock (G.M.T.) with their injections and meals until they get to their destination, when they can adjust their life to the altered time. They should always have with them a good supply of sugar to take in the event of airsickness, which can quickly lead to hypoglycaemia. The airline medical department should be informed of the dosage of insulin needed, also of the results of the last blood-sugar test and whether the patient is subject to hyperglycaemic or hypoglycaemic attacks. An oxygen set is provided for any diabetic known to be travelling, as they are sensitive to oxygen deficiency.

Thyrotoxicosis.—Patients with hyperthyroidism are not adversely affected by air travel unless there is fear of flying, in which case sedatives should be prescribed. Those with auricular fibrillation should not fly.

Gastro-intestinal Conditions.—Those with active *peptic ulceration* should be warned against air travel, owing to the danger of gaseous distension causing a haemorrhage or perforation. Patients whose ulcers have perforated or bled should not travel by air within two months of the event, and then only at an altitude not greater than 8,000 ft. (2,400 metres). Before each day's flight all peptic ulcer patients should be given hyoscine to prevent airsickness and to lessen peristalsis, and carminatives to counteract flatulence; they should follow their dietetic regime. After simple *abdominal operations*, such as appendicectomy or herniotomy, patients should not travel within ten days of the operation; after major procedures like gastrectomy or gut resections they should not travel for six weeks. Those with *hernias* should not travel by air unless the hernia is fully controlled by a truss or belt, as the hernia may become incarcerated as a result of distension of the gut. Patients with *liver abscess* are generally not acceptable owing to the liability of the abscess, if large, to burst. Those with *hepatic cirrhosis* should be rejected if there is evidence of congestive failure, haemorrhage, ascites, or hydrothorax.

Mental Disorder and Epilepsy.—Mental and epileptic patients are not normally accepted, but they may be in special instances when sedated and accompanied by a doctor or nurse. It is most important that they should not have alcohol, either just before or during the flight, or at stops *en route*, and the captain of the aircraft should be so informed.

Nephritis.—Nephritics are acceptable, provided there is no severe degree of anaemia, marked albuminuria, ascites, or hydrothorax, nor gross change of the optic fundi, and that the blood urea is not more than 100 mg. per 100 ml.

Respiratory Disorders.—Patients with respiratory disease require careful assessment before an air journey. Breathlessness on exertion is a good guide to their fitness or otherwise. If acceptable they should be instructed to move about as little as possible while in the air, and oxygen should be available for immediate use. *Asthmatics* must be considered individually. The condition of milder cases may be improved by flying, but those who suffer from severe attacks, especially if there is a cardiac or renal basis, should not travel by air, as an asthmatic attack is very disturbing to other passengers. In addition, inquiry should be made about any allergy to pyrethrum, as this is an ingredient of all insecticides used in aircraft. *Bronchitic* and *emphysematous* patients and those with fibrosis or neoplasm of the lung must be assessed according to the amount of lung tissue involved, the degree of dyspnoea, and whether there is offensive sputum, any cardiac lesion, or anaemia. Those who have had *lobectomies* or *pneumonectomies* should not travel within three months of operation, and even then the flight should not be longer than five hours at a maximum altitude of 5,000 ft. (1,500 metres). Those with *acute pneumonia* should not normally be accepted within a month of onset, as they are already anoxic in some degree, depending on the extent of lung involved. If such a case is carried, oxygen should be administered continuously from leaving the ground, for if anoxia develops it will be irreversible. Patients with active *pulmonary tuberculosis* are unacceptable, unless their sputum is free from tubercle bacilli and any cavity is controlled by collapse therapy. They should not, however, travel within a week of a refill, as the expansion of the air in the pleural cavity may tear adhesions and so cause haemorrhage and spread of infection. The lung must be at least three-quarters expanded in cases in which the mediastinum is fixed. Pneumoperitoneal refill cases should not have more than 2,000 ml. of air introduced, and there should be an interval of at least seven days between refill and flight.

The Extremes of Age and Pregnancy

Babies and *young children* travel by air as well as do adults, except that children get excited and move around a lot and tire themselves, with the result that they are more prone to airsickness; their highly sensitive labyrinths doubtless play a part in this. To prevent otitic barotrauma mothers should be told to give the baby a dummy or a feed during descent and to give the older children sweets to suck (see last week's Refresher Course article). There is privacy in the ladies' toilet on aircraft and in the rest-rooms at most airports, so babies can be breast-fed. If the baby is bottle-fed the mother should be advised to take with her an adequate supply of dried milk, bottles, and teats, though these can be supplied by the airline if due notice is given. Should it be decided to change over from breast-feeding to bottle-feeding for the journey, the change should be made gradually for a week or so beforehand. Bottles and teats can be cleaned and sterilized on board, and the stewardess will help look after the baby's wants. The mother should carry a good dusting powder and some calamine lotion for the baby's use in hot climates to prevent the development of heat rashes and prickly heat.

Elderly people travel well by air if they are free from organic disease. Those over the age of 65 should be advised to have a medical examination before undertaking a long flight for the first time, to ensure that they are not suffering from any marked degree of anaemia or cardiovascular disease or from incontinence of urine or faeces. They should be instructed not to move about in the aircraft more than is necessary, and to attend to their toilet so far as possible while on the ground. If the airline is told that an elderly person is travelling, arrangements are made to allot a seat near the toilet and oxygen is provided in case of need.

Pregnant women should undergo a medical examination and obtain advice before undertaking a journey by air. The doctor consulted should know the proposed flight plan, its expected duration, and the maximum altitude likely to be attained. Weather conditions are a minor problem now that most long-distance flights are made in pressurized aircraft which usually fly above the weather. The difficulties of attending to a confinement or an abortion while in flight will be appreciated, so the question of the date of expected delivery and the possibility of abortion must be carefully assessed. If there is evidence of threatened or repeated abortion, eclampsia, or severe morning sickness or travel-sickness, an air passage is inadvisable. Long-distance flights without night stops may be fatiguing, and it may be desirable to break the journey for a day or so *en route*. International airlines accept pregnant women up to the end of the eighth month, provided they are in good health and that oxygen is available for emergency. When it is known that a passenger is pregnant, she is given an anti-airsickness tablet before flight and she is allotted a seat facing backwards if available, so as to avoid any tension from the retaining belt at take-offs and landings. In addition, the captain and chief steward are informed, so that the maximum consideration can be given to her comfort.

Medical Arrangements made by the Airline

In the case of invalids the medical department of the airline sends to the patient's doctor or to the hospital concerned a special form ("medical certificate of fitness for air travel"). This raises a number of questions about the patient's medical condition, and the information given assists the medical department in assessing fitness for travel and in making arrangements for the patient's care, comfort, and treatment at the airport of departure, on the aircraft, and at the airport of arrival.

If the case is acceptable the medical department issues a "medical requirements certificate" to those concerned, to ensure that proper arrangements are made for the patient all along the route and that enough information is available to the captain of the aircraft or to any doctor who may have to be called in. The patient's doctor is told about these arrangements, and is asked to make sure that the patient has all the drugs needed for the journey and fully understands his instructions, which should be written clearly. The drugs and instructions may be given to the patient or passed to the chief steward for custody.

Medical Emergencies in Flight

If there is no doctor or trained nurse on the aircraft and an invalid's condition worsens during flight, or an ordinary passenger becomes ill to a degree beyond the skill and resources of the steward or stewardess (all of whom have had training in first aid as applied to aviation), the practice is for the captain of the aircraft to radio to the nearest port of call. He can then give details of the patient's condition and ask for medical advice on treatment during the flight or for special facilities to be ready on arrival.

Every airliner carries first-aid kit for emergency use, but considerations of weight and space demand strict limitation to really essential items. The commoner items included are bandages and dressings, analgesics, anti-burn creams, antiseptics, cardiac stimulants, laxatives, narcotics, and sedatives. In addition, the stewardess of each aircraft is provided with a medical hold-all which contains all items (other than dangerous drugs) that have been found necessary for day-

to-day treatment of minor conditions of illness. It is impracticable, however, to cater for everyone's whim and fancy, as to do so would convert the aircraft into a flying chemist's shop, so again only essentials are provided. Passengers, invalid or otherwise, are expected to bring with them their own particular medicaments.

A special oxygen set is provided, on the doctor's orders, for any invalid or elderly person who might be in need of it. It is fitted with masks to fit babies, young children, and adults. A stretcher cot, designed to facilitate loading on and off the aircraft and to give the comfort of a bed while travelling, is provided for those needing more than an ordinary stretcher. It is shorter than the standard stretcher and fits more easily across the seats of an aircraft.

Statistics

It is impossible to estimate the real number of invalids who travel by air, as usually only those who are severely disabled or anxious reveal their condition to the airlines. Certainly the number of known invalids travelling long distances has increased rapidly during the past three years, though they form only about 0.3% of the total number of passengers. For instance, in the B.O.A.C. some 900 known invalids are now accepted yearly, approximately half being for one-stage flights of under five hours and the others for long-haul flights of six hours to two days or more. In the past six years, when over a million passengers have been transported an average of 3,000 miles (4,830 km.) each, there has been only one case of natural death while in flight among these known invalid passengers, and one among all other passengers. There have, however, been two or three deaths yearly within 48 hours of completing an air journey among passengers who had not revealed their disability. The primary cause of such deaths was cardiovascular disease in the majority of cases.

Most passengers who have needed medical attention during flight (about 90 a year) have not been known invalids at the time of embarkation, the ratio being 12% known to 88% unknown. Most of these episodes have occurred in flights of six hours or more.

Conclusion

It is desirable for all invalids who intend to undertake a long air journey to consult their doctors, so that appropriate advice may be given and suitable arrangements made for their own good. It is unfair for them to expose the airlines and fellow travellers to delays *en route* and the unpleasantness of alarming episodes. Experience shows that even severely ill patients can safely travel long distances by air in pressurized aircraft, provided they are selected carefully and proper provision is made for their care and comfort.

Next Refresher Course Article.—"Convulsions in Childhood," by Dr. Bernard Schlesinger.

The seventh report of the Joint Committee, Order of St. John and the British Red Cross Society, discloses a sound financial position. A sum of nearly £10,000 was spent on relief services for prisoners of war in North Korean hands. The provision of library services in hospitals continues with good effect and increasing demand. Five bungalows given by the Pilgrim Trust and five provided by the Bernhard Baron Trust have been completed at the Settlement for Paraplegics, Garston, near Watford. A further grant has been made by the committee for the construction of eight more bungalows. With the assistance of the Royal Colleges of Nursing and Midwives and the Queen's Institute of District Nursing, the award of scholarships to nurses for postgraduate courses was continued, 27 awards being made during the year. Assistance has been given to 85,000 ex-Service men and women who required help in circumstances arising from their disablement.

PULMONARY TUBERCULOSIS IN CEYLON

BY

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Early in 1951 the Governor-General of Ceylon, Lord Soulbury, realizing how serious was the extent of pulmonary tuberculosis in that country, suggested to the Ceylon Government that advice on the problem should be sought from the British Isles.

It was thought that the first move should be the setting up of a thoracic surgical unit at Welisara Chest Hospital, near Colombo. Under the Technical Co-operation Scheme of the Colombo Plan an invitation was addressed to me by the Government of Ceylon to establish the unit. Arrangements for my visit were made by the Commonwealth Relations Office.

On my arrival in Ceylon it was at once clear that the then gross shortage of nurses and the absence of radiographic, pathological, and other services at Welisara Chest Hospital ruled out the immediate possibility of the formation of such a unit there. I accordingly suggested to the Prime Minister that the opportunity might be taken for me to carry out a general review of the thoracic services of the island, with special reference to tuberculosis, and also that I should set up the first thoracic unit at Colombo's teaching hospital instead of at Welisara.

First Thoracic Unit

Thanks to the ready co-operation of the Ceylon Government and the university and hospital authorities, I was quickly able to establish a thoracic unit at the General Hospital, Colombo, equipped with all modern facilities, and I performed a considerable number of thoracic operations there. Since that time the unit has been functioning very satisfactorily, first in the charge of a Scandinavian team, and, at present, under Mr. Abbey Smith, thoracic surgeon to the Warwick Group of Hospitals, with a team comprising an anaesthetist (Dr. L. O. Mountford), a surgical registrar, a ward sister, and a physiotherapist. Mr. A. T. S. Paul and another surgeon from Ceylon are now working with the team, and are expected to take over the unit after further training. The present team is to remain for six months, and it is hoped that the Commonwealth Relations Office will persuade the Treasury to finance a further first-class British team there before the unit is finally handed over. The formation of other units is planned.

Results of the Survey

Once the Colombo unit had been established the wider issues of thoracic services in general were carefully studied in relation to economic and other matters, and at the invitation of the Prime Minister the findings were reported in a White Paper.*

The conclusions and recommendations were the result of an island-wide survey. It was estimated that there were some 200,000 patients with active pulmonary tuberculosis out of a total population of 7.5 millions. At the time of the survey about 3,000 beds were allocated for these cases. The problems studied were, and still are, very serious indeed. The gross overcrowding in hospitals, with as many patients lying on the floor as upon the hard beds, the pathetic lack of nurses so that it was not unusual to find more than 100 patients in all stages of tuberculosis in the charge of one heroic nurse, the lack of rest and of any real treatment for tuberculosis, and the poor state in general of radiographic and pathological facilities, as well as many other matters of equal gravity, could not fail to demand notice. These diffi-

culties were described in the White Paper, and measures for dealing with them suggested. The Ceylon Government accepted the document in full and at once set out to implement the recommendations. Subsidies for the dependants of all tuberculous patients, improved living conditions, extension of hospital bed accommodation, training of doctors and nurses, and many other measures are now agreed and are developing. The Governments of Great Britain, Australia, and other countries are giving substantial financial aid. There is every indication that Ceylon will lead the East in the terrible battle against tuberculosis.

How the West May Help the East

Later, having seen something of the corresponding problems in India, and having discussed the matter with Rajkumari Amrit Kaur and other authorities, it occurred to me that, if the work in Ceylon could be brought to a successful issue in reasonable time, measures which proved successful there might be adopted State by State, or even town by town, in India, Pakistan, and elsewhere. Hopeless as the tuberculosis problem may seem in these countries, where starvation vies with tuberculosis for the honours of death, it is less hopeless when viewed in the light of planning in relatively small areas. It cannot yet be dealt with on a country-wide basis.

In England, and more especially in the Scandinavian countries, and in the United States of America, pulmonary tuberculosis is under control. In 10 years' time I believe it will largely have died out in these countries. I then visualize a time, not so far distant, when it will be the duty and privilege of every chest surgeon to offer six months' to one year's service at the height of his career—say after 10 years' service in consulting work in England, America, or Scandinavia—to go to the countries of the East to do what he can to teach doctors and nurses on their own ground, and to lend a hand in curing tuberculosis and other thoracic disease. Such service, offered and accepted in the right spirit, is the only hope of cure for the millions of tuberculosis cases in the East, and then only if their economic state can be improved.

*Report on the Thoracic Services of Ceylon, with Special Reference to Pulmonary Tuberculosis. Published by the Ministry of Health and Local Government, Colombo, May, 1952. Price 80 cents (postage 15 cents).

Reports of Societies

THE PSYCHOLOGY OF EATING

On January 31 the Scottish Group of the Nutrition Society held a symposium on "The Psychology of Eating"* in the Marischal College, Aberdeen.

Professor REX KNIGHT, of the Department of Psychology, Aberdeen, was in the chair, and he opened the meeting by saying that modern research on eating illustrated five of the main features of contemporary psychology. First, anecdote and unverified speculation had given place to controlled observation and experiment. Secondly, it was now recognized that likes and dislikes in food, and the psychosomatic aspects of digestion, were partly influenced by unconscious factors—for example, among adults, as well as children, aversion from food was often an indirect aversion from something or someone else. Thirdly, studies of the relationship between temperament and physique all took account of attitudes to eating, as in W. H. Sheldon's description of his "viscerotonic endomorph" as one in whom "the digestive tract is king." Fourthly, the current emphasis on the influence of social factors was reflected in the stress laid on the influence of culture-pattern, group-dynamics, and other social forces on eating habits. Fifthly, psychological phenomena were being increasingly linked to the physiological mechanisms that underlie them.

Professor W. M. MILLAR, of the Department of Mental Health, Aberdeen, then reviewed the psychiatric implications of disturbances of eating and nutrition. Eating disturbances appeared as the cause, correlate, or consequence of most psychiatric conditions. They were usually related to the inner significance of the act of eating rather than to the qualities of particular foods. Most common was anorexia, which appeared typically in cases of depression and involutional melancholia. The general relation of emotions, and particularly of rage and fear, to gastric function had been general knowledge since the experiments of the physiologists on the development of conditioned reflexes and their analysis of gastric mechanism by means of sham-feeding and the use of the Pavlov pouch. Later studies had suggested that the old or "visceral" brain might still play a part as an organ of "affectivity" in the relation between rage and fear on the one hand and alimentary function on the other.

Aetiology of Peptic Ulcer

Professor C. F. W. ILLINGWORTH, of the Department of Surgery, Glasgow, recalled that the study of peptic ulceration had been marked by a succession of wild theories, dogmatically asserted. As a student he had been taught that the ulcer was certainly the result of bacterial infection of the teeth and tonsils—whose removal was essential. It was important to be certain that more modern theories were based on a sounder foundation. There was certainly strong evidence for believing that anxiety reacted on the stomach, whether in the headmaster's study or on the public platform, and observation in patients with gastric fistula left no doubt that changes in gastric motility and secretion could be caused by emotional stresses. But that was not by itself proof of the psychological causation of an ulcer in the stomach; it simply gave a good prima facie case for objective investigation. Some psychiatrists had suggested that peptic ulcer could be related to a history of disturbing childhood influences, such as the divorce of parents, but Kellock's recent survey gave no evidence of this. Others had related the onset of haemorrhages to period of acute psychological stress, but clinicians were not satisfied that this was always the case. However, it was generally agreed that the patients belonged to a single psychological type, anxious and underweight.

It was well recognized that perforated peptic ulcer had shown a steady rise in incidence since the beginning of the century, and this was commonly attributed to the increased psychiatric stresses to which twentieth-century man was subject. But twentieth-century woman was equally subject to them, yet it was interesting that the increasing incidence of ulcer was confined to men. The high incidence of perforation in London during periods of air bombardment had been attributed to psychiatric stresses, but a similar increase occurred in Glasgow before the raids began. Indeed, in Glasgow the severe raids were followed by a noteworthy fall in the perforation rate.

Contrary to general opinion, there was no foundation for the belief that men in certain occupations, such as bus drivers, were more prone to ulcers. The only possible exception was for foremen and managers—possibly this was explained by the promotion of those who were of the type that worried about, and looked ahead to, the future.

Anorexia Nervosa

Dr. C. F. ROLLAND, of the Department of Therapeutics, Edinburgh, said that anorexia nervosa was characterized by a fall in body weight resulting from an antipathy to food, and in this sense was the antithesis of obesity, though much less common. It followed the development of a morbid

*The papers given at the symposium will be included in the *Proceedings of the Nutrition Society*, which are distributed to members. Inquiries about the Society should be made to Dr. G. M. Bourne, London Hospital Medical School, London, E.1, or, in Scotland, to Dr. E. C. Owen, Hannah Research Institute, Kirkhill, Ayr.

mental state which was difficult to define. Although no longer thought of as either hysterical or obsessional, it was frequently associated with emotional frigidity and problems to do with the sexual functions of the mouth.

The typical patient was a young unmarried woman who remained active despite severe wasting and did not complain of her anorexia. Often the doctor was first consulted about the amenorrhoea, which was probably a direct result of the starvation. The breasts remained surprisingly well preserved, the pulse was slow, and the blood pressure low. Signs of specific food deficiencies were very rare. The treatment depended mainly upon sensible management, which included removing the patient from home and using every form of encouragement to get her to eat. Attempts to stimulate the appetite with drugs had not been successful, and A.C.T.H. led to a gain in weight only as the result of retention of salt and water. Despite a positive refusal of food it was sometimes possible to get the patient to take nutrients disguised as medicines. The psychiatrist was often a very real help in the management of these patients.

Hypothalamic Control of Appetite

Dr. J. M. WALKER, of the Department of Pharmacology, Oxford, spoke on the physiological effects of smoking. There was a general belief that the average smoker would put on weight if he stopped smoking suddenly, and this had received support from a controlled experiment. Undoubtedly the improvement of the palate made food more appetizing, but an urge to satisfy the habit of putting something into the mouth also played a part. Smoking also raised the blood-sugar level and inhibited gastric contractions, nicotine being the most likely pharmacological agent. These effects might in turn reduce the feeling of hunger, but alternatively it now seemed possible that nicotine might have a more direct action on the hypothalamus similar to that of the amphetamine series of drugs, which reduced hunger although they did not raise the level of blood sugar. In controlled tests smoking had also been shown to inhibit water diuresis in man, and there was good evidence that this was produced by the action of nicotine in liberating the antidiuretic hormone from the neurohypophysis. Habitual smokers appeared to develop a tolerance to this action of nicotine, so that the phenomenon probably had little practical significance.

Dr. G. C. KENNEDY, of the scientific staff of the Medical Research Council, then described some recent experimental work on the effects of lesions of the hypothalamus. This small area of the brain was intimately connected with the pituitary and possibly inseparable in function. Experiments in which the area was damaged with an electrode introduced from above, so as to eliminate the possibility of damage to the pituitary gland itself, had shown its important role in the control of appetite. Rats so treated began to eat ravenously and indiscriminately immediately on recovery from the anaesthetic, and their appetite continued until they had become grossly obese. The limit was reached when approximately 70% of their entire body weight was fat. After a period of severely restricted feeding until their body weight had returned to normal the abnormal appetite reappeared. No recovery of normal control of appetite had been observed, although the discrimination of the animals increased as they approached their apparently limiting weight. Operations in which a slightly adjacent area had been damaged had sometimes resulted in animals entirely losing their appetite, but it remained possible that this was due merely to a post-operative irritation of the hypothalamus; and none of the rats had survived long enough for such an effect to have worn off. These results inspired speculation on the normal stimulus to which the hypothalamus responded. There was some evidence that the area was chemo-sensitive rather than thermo-sensitive. Further work would be needed to define the other levels of the central nervous system which play a part in the control of food intake.

Nova et Vetera

A MEDIAEVAL PHYSICIAN

Ugo Benzi: Medieval Philosopher and Physician, 1376–1439. By Dean Putnam Lockwood. (Pp. 441. 60s.) Chicago: University of Chicago Press. London: Cambridge University Press. 1951.

The medicine of the Middle Ages is not a popular field of study and must remain a close reserve for historical specialists. But Medicine, as a coherent and intelligible system, can be traced backward for a mere 4,000 years of man's 500,000 years' sojourn on this planet. Therefore the period from Galen (died *c.* A.D. 200) to the Revival of Learning, about 1500—a quarter of the historic period—can hardly be treated in complete silence even in the most elementary history of medicine. However, the historian's difficulty is that, though more than amply provided with texts of this period, he has hardly any material on the circumstances of day-to-day medical life and practice in this great stretch of time. For this reason—and for this alone—Ugo Benzi, of Siena, is of importance, since for him, alone among mediaeval physicians, the records hitherto discovered are adequate for biographical purposes.

He was born in humble circumstances, committed a theft to obtain means for a medical education, rose steadily in academic status, passing from one Italian university to another, until in 1429 he reached the prize of professorial ambition with the chair of theoretical medicine and philosophy—the two were combined—at Padua. There he remained till called in 1431 to be court physician to the D'Este family at Ferrara, where he died in 1439. His medical services were much sought and he attained to an international reputation. The popularity of his writing may be gained from the fact that, in addition to numerous manuscripts, his works appeared in no fewer than 44 printed editions, the last being in 1620, when Harvey was still at work. And yet, to the modern reader, all that Ugo Benzi wrote must appear completely empty—mere froth and contentious word-splitting. How could such a man of words come to be regarded in his age and place as the finest exponent of what we should now consider a profession of action? This strange phenomenon Professor Lockwood explains in lucid detail.

The main importance of his work is that, for the first time, it provides a living picture of a mediaeval physician, for there survive not only a life of Benzi by his son, but many records of his activities, as well as large numbers of his "consilia." These characteristic mediaeval products are written records, supplied to patients of high standing, expounding their condition—sometimes in great detail—and giving advice for regimen of living and of drugs. So exhaustive a collection has been made for no other mediaeval physician, and the annals of medicine are the richer for Professor Lockwood's patient and very skilled studies.

But economists have made us familiar with "the law of diminishing returns." However profitable a transaction or process, there comes a time when its gainfulness ceases to advance and begins to recede. So with all activities and, indeed, so with life itself. The law holds in the world of learning. All this is, perhaps, but an elaborate way of saying "anything can be overdone." Valuable as is this account, on which its author has worked for twenty years, its interest would have been more generally recognized had he compressed it into half of its 450 very closely printed pages, many of which would have been almost as useful to specialists if replaced by a line of reference. As it is, the book will certainly be a *locus classicus* for medical historians but not often perused by the "curious reader."

CHARLES SINGER.

Correspondence

Because of the present high cost of producing the Journal, and the great pressure on our space, correspondents are asked to keep their letters short.

The Training of Chartered Physiotherapists

SIR,—In recent correspondence mention has been made of the training of physiotherapists, and we therefore think it would be of interest to your readers to have further information on this subject.

In accordance with HMC (51) 48, all physiotherapists trained since January, 1952, and wishing to work in the National Health Service must hold the qualification of the Chartered Society of Physiotherapy. This qualification is open to those who have undertaken a three-year course of whole-time training at one of the 30 schools approved by the Chartered Society, and who have passed the Society's examinations. All the training schools are attached to hospitals in which clinical experience is gained. Students of physiotherapy study anatomy and physiology, massage, manipulations and movement, basic physics and electrotherapy, medical and surgical conditions, and appropriate techniques to be applied thereto. Their training is carried out by experienced chartered physiotherapists holding the Chartered Society's teaching qualification and by members of the medical profession. Their examination is similarly conducted by Chartered Society of Physiotherapy teachers and by professors of anatomy and physiology and members of the medical profession who possess one or more of the following qualifications: M.D., F.R.C.P., M.R.C.P., M.S., F.R.C.S., M.R.C.O.G.

Only by maintaining the high standard of its training and examinations can the Chartered Society ensure an adequate service to the patient, and to this end it looks for, and feels sure it will receive, the support of the medical profession, under whose direction all chartered physiotherapists are pledged by their ethical by-laws to work.—We are, etc.,

HARRY PLATT,
President.
PEGGY BARRON,
Vice-chairman of Council.

The Chartered Society of Physiotherapy, London, W.C.1.

Trichlorethylene in Labour

SIR,—Mr. E. E. Rawlings (February 21, p. 436) is to be congratulated upon his excellent article, and particularly on the painstaking details of his observations. As the Steel inhaler has been mentioned, may I say a few words on the place of trichlorethylene in obstetrics?

I am becoming increasingly convinced that we are wrong to try to replace the use of nitrous oxide and air by giving an unvarying concentration of trichlorethylene throughout, or for the greater part of, labour. First, this is contrary to one of the basic principles of good analgesia—that the degree of the analgesia, or the nature of the drugs used, should vary in accordance with the intensity and the nature of the pain stimuli. The pains of labour vary in degree, in intensity, and in nature; and an unvarying amount of any one drug will be too much at one time and too little at another. The result of giving this fixed amount is that after some time the increase in the pain stimulus lowers the efficacy, or the patient's appreciation of the efficacy, of the analgesia. This is shown by the fact that gas and air, when started towards the end of the first stage, frequently seems ineffective at the time of delivery. It is confirmed by Table V in Mr. Rawlings's series, which shows that the degree of dissatisfaction with the trichlorethylene analgesia increases with its duration. In the case of trichlorethylene there are further disadvantages to prolonged administration. It has been shown to have a cumulative effect. My own observations that a somewhat sluggish action of the uterus may occur are confirmed by the increase of duration of labour in Mr. Rawlings's series, and by his conclusion that it may cause uterine inertia if started too soon. It is thus clear that we must eschew the idea of allowing the midwives to give trichlorethylene over a long period, no matter how unvarying the concentration; and we must completely reorientate our ideas as to how and when it shall be given.

The first essential is that there must be a time limit on the administration of this drug in each labour, and that it must be used to *supplement, not to replace,* nitrous oxide and air. Provided that the administration is properly supervised, gas and air will give adequate and safe relief of pain in most cases from the latter part of the first stage until the passage of the head over the perineum. It then becomes ineffective, for the reasons that I have outlined. Since we cannot increase the strength of the gas and air, we must change the nature of the drug. It is at this point that the use of trichlorethylene can be realized to its full advantage. Not only is there a change to a different and a more effective drug, but also the short time for which it will be given avoids the possible disadvantages of its prolonged use—the patient's acclimatization, or sluggish uterine action. This time limit on the use of the drug can best be imposed by limiting the amount of trichlorethylene that the midwife may carry, and it was to this end that the Steel inhaler was designed.

A crushable brisette containing 3 ml. of trichlorethylene is broken and slipped into a perforated carrier in the inhaler. The jacket of the brisette takes up all the liquid so that none can be spilt: this lasts on an average for 15–20 minutes. Preliminary tests showed an inhaled concentration of 0.45 vols.%, with a variation of 15%. Provided that the amount of trichlorethylene is thus restricted, the harm that may accrue from this variation, or for that matter a much larger one, is much less than the mounting evidence shows to be the case when administration is prolonged, even though the concentration is kept constant. The crux of the problem is the control of the amount that the patient may be given. If the drug could be put on a restricted list so that the midwife is permitted to carry two brisettes, as in the case of pethidine, she could use them in the inhaler in the last phase of labour in succession to gas and air. Thus the benefit of both drugs would be reaped without the weakness of the one, or the disadvantages of the other, being incurred.

The fundamental weakness in our approach to obstetrical analgesia has always been that we have demanded too much from each newly evolved method. It would be a tragedy if the very just claims of trichlorethylene as an obstetrical help could not be realized owing to lack of appreciation of how and when to use it.

Pethidine controlled in amount, then gas and air controlled in concentration, and, finally, trichlorethylene controlled in *amount* (and thus in time) as well as in concentration should be our aim.—I am, etc.,

G. C. STEEL.

London, S.W.15.

Perforated Peptic Ulcer Mortality

SIR,—I would like to congratulate Drs. F. Avery Jones and R. Doll upon their excellent and stimulating article on the treatment and prognosis of perforated peptic ulcer (January 17, p. 122).

Our experience at the General Infirmary at Leeds does not support the view expressed therein that the operation mortality has yet reached the low level of 5%. During the five-year period 1948–52 inclusive, 535 patients suffering from acute perforated peptic ulcer were admitted. Of these, 439 were operated upon and 32 died—a mortality rate of over 7.2%. Taking the two most recent years, 1951 and 1952, the figure is just over 8%. Of the remaining 96 patients, elective conservative treatment was adopted in 82 with two deaths, whilst 13 were *in extremis*, so that forced conservative treatment was all that was deemed possible, and all 13 patients died. The overall mortality rate for the past five years has been 47/535—that is, 8.8%.

The most important factors influencing mortality in perforated peptic ulcer are still the interval of time between perforation and the commencement of treatment and the age of the patient. In the most favourable group of patients—those treated within 12 hours of the perforation and under 50 years old—there have been during this quinquennium four deaths out of a total of 245; three of these died from general peritonitis with bronchopneumonia (second, fourth, and fifth post-operative days), and one from bronchopneumonia on the seventh post-operative day (all verified by necropsy).

We have found in Leeds that general peritonitis still exacts by far the greatest toll of deaths in perforated peptic ulcer. Our experience does not support the view that "deaths from peritonitis in the first week have almost ceased to occur." All the 47 deaths referred to above were subjected to necropsy and the cause of death reported as follows: 26, general peritonitis, only two occurring later than the seventh day (on the tenth and twentieth days); 7, general peritonitis associated with serious lung complications, only one occurring later than the seventh day (on the eighth day); 3, general peritonitis and heart disease; 1, pulmonary oedema and congestion, tenth day; 8, haemorrhage; 1, pulmonary embolism, twelfth day; 1, death under anaesthesia.

It will be seen, therefore, that general peritonitis was the important factor in no less than 36/47 patients—that is, over 75%—and all but four of these patients died during the first week. A further reduction in the mortality rate of acute perforated peptic ulcer, under present conditions, would appear to depend on earlier diagnosis and still earlier treatment, possibly in the direction of conservatism.—I am, etc.,

Leeds. GEORGE ARMITAGE.

Tuberculin-testing of Infant-school Children

SIR,—To appreciate the proper place of the article by Drs. I. A. MacDougall, J. R. Mikhail, and W. H. Tattersall (January 10, p. 64) in the history of the "jelly test" in Bournemouth, it is necessary to refer to "The Tuberculin Jelly Patch Test in Infant Welfare Centres and in the School Medical Service: A Preliminary Report" (F. A. Heimann and H. R. Paterson, 1945, *Med. Offr*, 74, 209). These two doctors reported on 810 cases which they had personally investigated and from which they drew several important conclusions. Among these conclusions were (1) that the jelly test should be carried out as a routine on all schoolchildren and in infant welfare centres, and not only on contacts; and (2) that positive reactors should be fully investigated by *x*-ray examination, etc., as having been infected by the tubercle bacillus at some time. This article was the first indication that experiments of this kind were being carried on in the borough—experiments which have been continued by these authors ever since.

The report published in the *Journal* emphasizes the possibility of tracing the source of tuberculous infection in positive-reacting young children. Until children were protected by clean milk supplies this task was almost impossible. It is gratifying to all interested in the fight against tuberculosis to know that the jelly test has now received official recognition in Bournemouth as a weapon to defend children against tuberculosis from either human or bovine sources by bringing to light unsuspected foci of danger.—I am, etc.,

Bournemouth. P. P. MCKINNEY.

Tuberculous Aliens in St. Pancras

SIR,—On Tuesday, February 10, several morning papers carried a paragraph which alleged that a quarter of the patients attending the St. Pancras Chest Clinic were aliens, and that this was a reason for *x*-raying the chests of all immigrants. The day before at a meeting of the North-west Metropolitan Regional Hospital Board, to which reporters were admitted, some figures were discussed which had been provided by the St. Pancras Chest Clinic. These figures were not to show the number of aliens but to give a rough guide to the racial distribution of patients (1) attending the clinic and (2) on the notification register in 1952. It is reasonable to suppose therefore that they formed the basis for the paragraphs. The figures, given below, were obtained by picking out names which suggested a racial origin other than English, Scottish, or Welsh, and no attempt was made to find out whether the owners of the names were, in fact, aliens or how long they had been resident in this country. No evidence whatever was obtained to show what proportion, if any, arrived in this country suffering from tuberculosis.

Metropolitan Borough of St. Pancras

Race	*New Patients*	*On Register*
Irish	123	87
Italian, French, Spanish	39	37
Middle European	27	17
Cypriot and Greek	25	30
Indian and Pakistani	9	10
Chinese	7	2
Polish	5	12
African	3	3
Others	762	802
	1,000	1,000

It may be thought that the Press misinterpreted the information which they obtained at the meeting, but in the Londoner's Diary of the *Evening Standard* on Wednesday, February 11, the following paragraph was published: "Doctors treating tuberculosis in Britain are disturbed at the prevalence of the disease among aliens coming to work here. Dr. Horace Joules, medical director of the Central Middlesex Hospital, tells me that a quarter of the patients at his chest clinic in St. Pancras are aliens. Many of them work in catering and the licensed trade. He fears that preventive work against the disease may not succeed for many years if aliens are allowed to enter with undiscovered tuberculosis." When I inquired from the editorial department where they obtained this information I was told that, having seen the paragraph in the previous day's morning papers, they had confirmed it by telephoning to a member of the North-west Metropolitan Regional Hospital Board.

I am drawing attention to this to show that the facts as stated about St. Pancras are very misleading; to suggest that information of this kind should not be handed to the Press without consultation with the department by which it has been provided; and to point out that, whatever the merits or demerits of *x*-raying the chests of immigrants, the St. Pancras figures are not relevant.—I am, etc.,

London, W.1. G. A. BACK.

Mosquitoes and the Floods

SIR,—Many minor problems will arise from time to time following the recent floods along our East and South coasts, and one which will cause the local authorities some concern will be mosquitoes. For many years past marked increases in the number of mosquitoes have occurred following exceptionally high tides when the sea wall has been breached or where the sluice-gates have not operated properly.

At some time or other during the past 21 years local authorities of most of the areas now affected by the floods have found it necessary to carry out mosquito control operations, sometimes on a fairly large scale. In every case a single species of mosquito, *Aedes detritus*, has been the cause of the nuisance. Although some other species are able to breed in brackish water, *Aedes detritus* is the only British species which breeds exclusively in brackish water. The larvae are able to breed in water which has three or four times the salt content of the sea itself, and this is often the case beyond the sea wall owing to water evaporation between very high tides. In these waters larvae of *Aedes detritus* are often present in enormous numbers. All our British species of mosquitoes have a resting phase of several months either as eggs, larvae, or female adults, varying from species to species. *Aedes detritus*, however, continues to breed throughout the year, although reproduction is low in the winter months. Numerous surveys in coastal districts over the past 25 years have shown that the prevalence of

this species in a given area is dependent on the suitable breeding-grounds available. In addition to the great increase in the expanses of stagnant brackish water owing to the recent floods, many dykes, ditches, and ponds which were formerly filled with "fresh" water have now become brackish and will add considerably to the breeding potential of *Aedes detritus*. There may not be an immediate increase in the *Aedes detritus* population, because for a while the small marine animals will prey on the larvae, but these creatures will soon die and it will be then that the increase in the mosquito population will occur. It is well to remember that it is often not the large expanses of water which form the principal breeding-grounds, but the small "pot-holes," often far beyond the foreshore.

It is to be hoped that local authorities will see that their sluice- or tide-gates work efficiently and that any drainage work will be carried out in such a way as to prevent the persistence of large numbers of brackish water puddles.—I am, etc.,

Malaria Reference Laboratory, Epsom. P. G. SHUTE.

REFERENCE

Memorandum on measures for the control of mosquito nuisances in Great Britain. Memo. 238/Med., 1949. H.M. Stationery Office. Price 9d.

Abuse of Antibiotics

SIR,—The correspondence which followed the publication (December 13, 1952, p. 1307) of my letter on "The Abuse of Antibiotics" has proved both interesting and informative. Especially valuable is the contribution of Professor F. A. R. Stammers (January 31, p. 272) in indicating the modifications of the general body reaction which occur under the influence of these medicaments.

The letter from Mr. N. N. Iovetz-Tereshchenko (February 21, p. 454), however, criticizes the conduct of the case of appendicitis which I quoted in my letter, so that I feel some vindication is necessary. I agree, of course, that there can be very few cases nowadays in which it is either justifiable or necessary to leave the appendix, but this happened to be just such a case. As it was quite irrelevant to the subject of my letter, I did not think it necessary to explain that the reason for the delay in making a diagnosis in this case was almost surely the fact that the youth concerned had complete transposition of all his viscera, so that in the earlier stages his signs and symptoms had been left-sided. The pelvic abscess which ultimately ruptured into the general peritoneal cavity was also confined to the left side. At the time of operation, in a desperately ill patient, it would, in my judgment, have been foolish to spend time dissecting a buried appendix out from a mass of inflammatory material in the pelvis—hence the decision to drain. The youth recovered without the formation of a fistula or sinus, so that this course has been justified by events. His appendix is to be removed shortly.

Incidentally, it is of interest to know that it was subsequently learned that this patient had had a routine chest *x*-ray examination at his works some time previously and that the transposition of the heart had been noted. The youth, however, had not been informed of this, nor were any further examinations done to see if his other organs were also transposed. Had his doctor been aware of this finding, it is probable that the delay in the diagnosis of appendicitis would not have occurred. The moral is obvious.—I am, etc.,

London, W.1. NORMAN C. LAKE.

Butazolidin

SIR,—Your leading article on the dangers of "butazolidin" (December 27, 1952, p. 1401), and the ensuing correspondence, prompt me to report a fatality which appeared to be due to the use of this drug in a case of gout.

The patient, a railway clerk aged 55 years, had suffered from an intermittent polyarthritis for 15 years, most of his large joints having been affected and the metatarso-phalangeal joint of his right big toe also on one occasion. In December, 1949, his serum uric acid was 11.4 mg. per 100 ml., and in the following February it was 7.9 mg. per 100 ml. Previously it had been reported as raised on two other occasions. His father had had one attack of podagra, and his grandfather had had numerous attacks. Early in the new year the patient had a recrudescence of symptoms, with severe pain, and his doctor prescribed butazolidin two tablets three times a day (1,200 mg. daily). The pain was dramatically relieved, but on the fourth day of treatment, after 16 tablets had been given, there was a painless haematuria, which lasted for two days. Administration of the drug was stopped at once and the patient was given a simple alkali mixture and one dose of a purgative. Within a few days an oliguria was noticed, and, apart from an occasional slight remission, it became progressively more severe. On the ninth day after the first dose of butazolidin the patient became dyspnoeic. There was an almost complete anuria on the eleventh day, at the end of which he was admitted to hospital at 10.30 p.m. On admission the patient was of good colour, his face being slightly flushed, but he was breathless and anxious. The tongue was brown and dry, and the eyelids were puffy. There was slight oedema of the sacral pad. The blood pressure was 185/100 mm. Hg, temperature 98° F. (36.7° C.), pulse 96, and respiration 26 per minute. Half an ounce (14 ml.) of urine only was obtained by catheter. Three hours later the condition appeared unchanged, but as his temperature was about to be taken the patient suddenly died.

I performed a necropsy three days after death. There was an acute bilateral hydronephrosis and hydroureter, each ureter measuring 2 cm. in diameter at its upper end, tapering down to 1 cm. in diameter at its lower end. The ureters narrowed abruptly as they entered the bladder wall, and they were of normal calibre from this point onwards. A tight plug of yellowish-brown granular material measuring about 1.5 cm. in length and 0.8 cm. in diameter was found in the lower end of each ureter, just above its point of entry into the bladder wall. This material was sent to the county analyst, who found it to consist mainly of uric acid, with a lesser quantity of urea; and he excluded the presence of butazolidin. Similar granular material was present in both pelves and in all the calyces, but there were no formed calculi. The kidneys were both moderately enlarged, and each weighed 240 g. The pelves and calyces were dilated, but the renal parenchyma was not reduced in thickness. Histologically the kidneys showed no chronic lesion apart from a focal lymphocytic infiltration and an occasional fibrosed glomerulus. There was no fibrosis of the stroma and there were no areas of cellular reaction around crystalline deposits. It seems, therefore, and the coroner so found, that the drug caused an acute precipitation of uric acid (or one of its salts) in the urinary tract, either by producing a concentrated urine by retention of water in the tissues, or by inducing a massive excretion of uric acid.

This case suggests that when using butazolidin in the treatment of gout a special watch should be kept for the onset of oliguria. If it happens to be due to obstruction of the urinary outflow, as in the case here reported, ureteric catheterization and irrigation may be a life-saving procedure.

I wish to thank Mr. J. A. Johnson, H.M. Coroner for the Borough and Liberties of Dover, for sending me a copy of the depositions.—I am, etc.,

Folkestone. V. H. BOWERS.

Use of Succinylcholine in E.C.T.

SIR,—We welcome the letter of Drs. J. A. Smith and F. G. Wood-Smith (February 21, p. 451), as it enables us to make an acknowledgment. Two other papers have been published which mention the effects of succinylcholine on blood pressure. Malone and Blayney[1] stated that, although they had not recorded the blood pressures of their patients, no change was observed clinically. McDowell, Rahill, and Tyndall[2] measured the blood pressure before and after the injection of succinylcholine, and found an increase of about 40 mm. Hg. Smith and Wood-Smith suggest that the rise of blood pressure was not due to the succinylcholine but to the administration of oxygen containing 5% carbon dioxide. This suggestion is disproved by the control experiments we described in which the procedure was repeated exactly except for the injection of sterile water instead of succinylcholine. In any case the blood pressure after the injection of the drug was taken before the oxygen mixture was administered. (Incidentally, we use pure oxygen now, as it is just as good.) We must apologize for the obscurity of the manuscript in not making this quite clear.

It is always possible that the rise in blood pressure is due to the accumulation of carbon dioxide during the period of apnoea. This is unlikely, as the second blood-pressure reading was taken as soon as the succinylcholine had exerted its full effect, usually less than a minute after injection. The period of diminished respiration is obviously much less. The hypothesis can be tested very easily in at least two different ways, but the onus of proof is upon those who proposed it. The advice of John Hunter to William Jenner is still good.—We are, etc.,

M. HAMILTON.
D. J. ADDERLEY.

London, S.W.17.

REFERENCES

[1] *Irish J. med. Sci.*, 1952, 65, 315.
[2] *J. Irish med. Ass.*, 1952, 31, 240.

Intra-arterial Injection of Thiopentone

SIR,—In the light of the recent correspondence by Dr. J. W. Dundee (February 14, p. 402) and Dr. J. N. Fell (January 10, p. 95) on intra-arterial injection of thiopentone, the following experience may be of interest.

An obese young woman of 21 was operated upon for acute appendicitis. Premedication consisted of "omnopon" 20 mg., and scopolamine 0.4 mg. one hour before operation. The needle of a 20-ml. all-glass syringe was inserted into what was thought to be the median cubital vein. After aspiration of a small quantity of red blood, 5 ml. of 5% thiopentone was injected. After pausing for a moment it was noticed that blood was spurting into the syringe, driving back the piston. The patient did not complain of pain, even when asked the leading question. No change in the colour or temperature of the skin took place, and the radial pulse did not alter in volume. No immediate treatment was given, as it was assumed that with the lack of pain and unaltered pulse volume no spasm of the arteries or arterioles could have occurred. The needle was withdrawn after about two minutes, and 0.5 g. of thiopentone was injected into a small median vein of the other wrist, anaesthesia being maintained with nitrous oxide, oxygen, pethidine, and tubocurarine. No change in the patient's arm could be detected during operation, but about three hours afterwards a slight mottling of the skin of the front of the forearm was seen. This disappeared within 24 hours and there were no further effects.

The following points of interest arise. The colour of the aspirated blood may be misleading, as venous blood may vary from almost black to quite bright red. This variability depends on the percentage of oxygen desaturation of the venous blood, which in turn is probably due to psychological factors acting before the operation. In a well-sedated patient with a relatively low cardiac output the venous blood returning from a limb will be considerably more deoxygenated than in an apprehensive patient with a relatively high cardiac output. In the case described, the fact that the aspirated blood was quite bright red was not considered of significance, with what might have been serious results. It is evident that 5% thiopentone solution can be injected intra-arterially without causing pain or spasm of the arteries. The importance of carefully observing the aspirated blood for pulsations in an unhurried manner is clearly indicated.—I am, etc.,

P. HEX VENN.

Chester.

Death after Intravenous Injection of Iodoxyl

SIR,—With reference to the report by Mr. G. S. Ramsay (February 21, p. 439) of a death following intravenous administration of iodoxyl, I should like to record a further fatality due to this substance.

The patient, a woman of 63 in good health, was being investigated for pain in the left loin and haematuria. Twenty ml. of "pyelectan" (iodoxyl) was injected into the right antecubital vein, four minutes being taken to give the injection. During this time she complained of faintness, and at the end of the injection said that she felt giddy and had a slight burning feeling in her throat. She looked flushed. Three minutes later she became restless and complained that she could not breathe. She sat up and then lay back in a collapsed state. There was a gurgling noise in the throat, but no marked expectoration. She rapidly became cyanosed and unconscious. Ten minutes after the end of the injection she was deeply unconscious, with a weak pulse, feeble respirations, and marked cyanosis. A diagnosis of peripheral circulatory failure was made, but it was also thought that she might have had a pulmonary or cardiac infarct. Six ml. of nikethamide was given intravenously and 1 ml. of 1:1,000 adrenaline subcutaneously, and oxygen was administered. Artificial respiration was started. No pulse or heart beat could be felt 20 minutes after the injection. Cardiac massage through an abdominal incision was then instituted, but the heart was quite inert, so this was abandoned after five minutes. At necropsy, death appeared to have resulted from circulatory failure presumably due to the injected material.

In view of the recent report[1] that deaths following intravenous pyelography have been due to the administration of diodone, I think it is important to record any deaths due to iodoxyl.—I am, etc.,

H. J. BARNES.

Cambridge.

REFERENCE

[1] *Lancet*, 1953, 1, 281.

Smoking and Lung Cancer

SIR,—Dr. R. Doll and Professor A. Bradford Hill (February 28, p. 505) mention one possible non-causal explanation of the relationship they have demonstrated between smoking and cancer of the lung. This is that subjects with a particular constitution may be prone both to smoking heavily and to carcinoma. Although I agree with them that the weight of present evidence favours taking preventive action now, I still think that the constitutional explanation deserves exploring. This could be done by taking certain physical anthropometric measurements, more especially height and bone width, in cancer patients and controls. In relation to height, mesomorphs have larger bones than endomorphs, and the measurements required are not subject to the vagaries of photographic interpretation of somatotype in ill people.

Apart from inequalities in smoking, Doll and Hill found more patients with carcinoma of the lung to have had a previous history of pneumonia and bronchitis. Among undergraduates I found smoking commonest where endomorphy and mesomorphy were both rated high,[1] but there are the additional facts that a history of pneumonia in childhood was commonest in endomorphic mesomorphs, a history of bronchitis in ectomorphic mesomorphs. In childhood, smoking seems a less likely cause of these diseases than, for example, the comparatively large air passages which mesomorphs enjoy. On the other side of the constitutional picture, women, who are mostly endomorphic, are found to suffer less from lung cancer. Lastly, if there is any truth in the suggestion that a habitual pipe smoker is usually a more contented person than a cigarette smoker, he may owe his contentment to a viscerotonic temperament, and his relative freedom from lung cancer to an associated and dominantly endomorphic constitution.—I am, etc.,

R. W. PARNELL.

Oxford.

REFERENCE

[1] *Lancet*, 1951, 1, 963.

The Medical Practitioner and the Law

SIR,—The growing number of medico-legal cases reported in the medical and lay press is very disquieting, but even more disquieting is the nature of the judgments pronounced. These are almost invariably unfavourable to the doctor, and not infrequently I have been unable to follow the reasoning that has led to the judgment. I realize that in the majority of cases the doctor does not suffer any financial loss, but he is subjected to considerable anxiety, loss of time, possible loss of practice, and his reputation is not infrequently smeared with an unproved charge of negligence. Some of these cases reveal a disturbing lack of support for the junior doctor by his senior and more experienced colleagues, some of whom appear to be a little out of touch with the problems of the newly qualified doctor working in a health service that has not as yet provided unlimited beds for all potentially serious cases. They appear to forget that many of us have not had the opportunity to benefit from their particular brand of teaching and practice.

With reference to the case reported in the *Journal* (January 17, p. 166), I find it difficult to understand why so little notice was taken of the medical opinion favourable to the casualty officer. By what strange mental process is it possible for Her Majesty's Judge to decide that certain physical signs were present but not detected when a medical examination was carried out by a duly qualified and competent doctor? Every doctor of experience knows that symptoms vary considerably and can be inexplicably absent on occasion. We are entitled to a better understanding of our difficulties and limitations.

It appears to me that we are now to be held liable in law if we commit an error of judgment that results in death or grave illness for one of our patients. This is surely a new departure, and, if so, must needs make every one of us more concerned to protect ourselves from possible medico-legal action and less concerned with the diagnosis and treatment of our patients. Some means must be found whereby the present position can be altered. Is it not possible for the medical and legal professions to evolve some form of procedure that would be fair, and be seen to be fair, to both the medical practitioner and his patient? —I am, etc.,

Bradford. G. A. CRAIG.

The Metric System

SIR,—It is fortunate for the progress of clear thinking and logical action that there are not many confusers of issues who write with such entertaining charm as Dr. C. Langton Hewer (February 21, p. 450), otherwise even the most level-headed might find themselves bewitched.

Dr. Hewer has succeeded in introducing at least two red herrings, and at least one major piece of disingenuousness, into an argument on what ought to be a fairly simple issue. Professor W. C. W. Nixon and Mr. T. D. Whittet (February 7, p. 327) advocate the metric system of weights and measures; even though by implication their argument, should it be found sound, would lead us towards adopting a new coinage, we are not called upon to consider mathematically precise extrapolations of their proposals. To your correspondents' plea for introducing grammes and millilitres in place of pounds, pints, ounces, drachms, and scruples of all kinds, Dr. Hewer replies, first, that it cannot be done, secondly, that people quarrel about abbreviations, thirdly, that there has been a difference of opinion on one metric unit, that of volume, and, fourthly, that some carefully selected figures are difficult, or even impossible, to remember. I do not propose to argue Dr. Hewer's first point, save to remark that it shows a degree of national modesty excessive even for a Briton, seeing that other nations have managed to use this system, so difficult to the minds of Dr. Hewer and his supporters, for decades.

I must, however, insist that any difference of view between those who use the cubic centimetre and those who use, more punctiliously, the millilitre as a measure of volume is merely an indication that one party is a good many years out of date. The *British Pharmacopoeia*, surely not an organ of revolutionary opinion, having adopted the millilitre and expunged the cubic centimetre from its pages as long ago as 1914, and the even more cautious *British Medical Journal* some years later, the question of which is the correct expression is no longer an issue; the question of which should be used in medical literature is one that is to be determined by several considerations. In these days of increased expectation of life, one has to wait longer and longer for the deaths of those habituated to outmoded expressions. No doubt the cc. will be dropped in this country when the last medical practitioner to have graduated before 1914 will be thought likely to have gone out of practice because he is over 90, but it does seem rather a long time to wait. In any event, the issue is one within the metric system and not one between that system and the apothecaries'. I presume that Dr. Hewer will not be so bold as to argue that the metric system has a diathesis making it inevitably liable to this kind of conflict and that our British system is gloriously free from such a disadvantage.

On the next issue, that of abbreviations, it can hardly be argued that changes in official practice, or differences between individual journals, are peculiar to the metric system. Seeing that the word "pounds," for example, may be abbreviated according to taste, and indeed all four variants are to be found, lb, lb., lbs, or lbs., and that similar differences arise with other abbreviations of English weights and measures, I think Dr. Hewer must console himself with the thought that this particular kind of vagary is one of the ills that medical and scientific flesh is heir to and that he has just got to lump it—if you will forgive the expression.

Finally, while agreeing that a drachm per stone body weight is easier to remember than 3.55 ml. per 6.35 kg., I suggest that Dr. Hewer and his supporters are not being subjected to an over-severe intellectual strain if asked to remember that the dose is one ml. per 1.8 kg. or even, as near as no matter, 5½ ml. per 10 kg. After all, use of the stone for body weights, which makes Dr. Hewer's particular instance sound so simple, is not a custom even among all English-speaking peoples, and its mention might well cause alarm and despondency in the United States. As to Dr. Hewer's rhetorical question about how many people could visualize a patient 1.895 metres high (who would hardly be distinguishable from another who was 1.900 metres high) and weighing 64.37 kg., I suggest that he asks the next French colleague he meets whether he can visualize a patient weighing 10 st. 3 lb. 2 oz., whose height is 5 ft. 9¾ in.

If, as I tend to fear the more I reflect on this matter, Dr. Hewer's letter was a magnificent leg-pull and meant as a parody of the kind of argument always put up by those who oppose progress to the last ditch, I can only apologize for my obtuseness—and am, etc. (not, I protest, etec.),

London, N.W.3. A. L. BACHARACH.

SIR,—We are surprised to find Dr. C. Langton Hewer (February 21, p. 450) such a determined opponent of the metric system, since, as an anaesthetist, he must find most of the drugs he uses are prepared in this system. Thus all the muscle relaxants, most of the local analgesics, and the newer analgesics are issued either as percentage solutions or as solutions containing a stated number of milligrams per millilitre. There is no doubt whatever that the metric system has come to stay in this country, and it will become increasingly used as new drugs are introduced. Even if we admit the disadvantages stated by your correspondent (and we consider them trivial) they will therefore continue along with the greater absurdities of the older systems. Surely no one would favour putting the clock back to the extent of abandoning the metric system and reverting completely to the apothecaries' and avoirdupois systems.

Dr. Hewer mentions that in many fields Anglo-Saxon production is greater than that of the rest of the world, giving this as a reason for retaining the old systems. This may possibly be true in pharmaceutical products, but does he realize that there is no agreement between British and American fluid measures? For example, an Imperial ounce equals 0.9608 U.S. fluid ounce, an American pint contains 16 fluid ounces (U.S.) compared with our 20 fluid ounces (Imperial), and one Imperial gallon equals 1.201 U.S. gallons. These anomalies, added to those of avoirdupois and apothecaries' weights, make points such as the spelling of the abbreviation for "millilitre" seem of small importance. It should not be difficult to reach agreement on such minor points. We do not think it would be much more difficult for doctors to learn half a mil. per kilo. than one drachm per stone of body weight as an approximation for paraldehyde dosage, and visualization of metric quantities becomes easy with practice.

Finally, if our suggestion of abandonment of the old systems is carried out, everyone will only need to learn the metric system instead of both, as any conscientious person must do at present. We should like to draw

Dr. Hewer's attention to the 1953 edition of the *British Pharmacopoeia* (published by the General Medical Council), in which the dosage of the newer drugs—anaesthetics, hormones, antibiotics—is given in the metric system exclusively. Those of the older drugs are now given in this system, but with the apothecaries' equivalents in parenthesis.—We are, etc.,

W. C. W. NIXON.
T. D. WHITTET.

London, W.C.1.

SIR,—The advocacy of the adoption of the metric system by Professor W. C. W. Nixon and Mr. T. D. Whittet (*British Medical Journal*, February 7, p. 327) will find much support among recent graduates, and it is overdue. Since we are to see changes we must ask ourselves whether the opportunity should not be taken to consider another aspect of the subject and let in an element of realism.

Dispensing by general practitioners during the past 20 years in all countries has undergone modifications. The doctor of medicine is now responsible only for deciding the quantity of any drug and for stating this in writing. What the patient receives in exchange for the written prescription lies entirely with the dispensing chemist, who in most cases dispenses what is sent to him from the manufacturing chemist under various labels. The doctor has neither the knowledge nor the time to analyse any of the medicines received by the patient. The doctor trusts the dispensing chemist to dispense the right quantities, and the dispensing chemist trusts the manufacturing chemist for the correctness and strength of the material dispensed.

Since it is no longer practicable for the prescribing doctor to be held responsible for either the ingredients or the quantity thereof in the tablet or bottle, the various signs and symbols indicating quantities employed in prescriptions by doctors have little real meaning beyond expression of a desire. In the "good old days" medicines were measured solely by volume or weight. To-day for some drugs we employ units or multiples thereof which have been announced as a dose by the producers, who are the only persons with the necessary knowledge of the proper and convenient dose of such drugs. At the moment we use units which refer to totally different quantities—for example, units of insulin, penicillin, and vitamins which are not comparable. In recent months we have been prescribing micrograms, which must tax the imagination of the prescriber. The profession has found no difficulty in accepting and adopting these innovations of unitary standards.

Surely the logical outcome of all this is the adoption of a unitary standard for all medicaments. Let us vest the task of standardization of units in some scientific body similar to that committee of the General Medical Council which at present controls the *Pharmacopoeia*. This committee should be composed of professors of medicine, pharmacologists, physiologists, practical chemists, and others competent to decide what is the effective dose of any drug for general use. The quantity decided upon for each drug by such a committee would be adopted as the unit for that drug. The advantages to the profession would be immense, and the adoption of such a plan would not entail much labour. We have already official dosages; for instance, calomel, the official dose being ¼ gr. to 3 gr.; the standard unit could be 1½ gr., based presumably upon average body weight. This would be prescribed "℞ calomel 1 unit" in the average case, with decimal fractions of a unit for children and multiples of a unit for exceptional cases, according to the desired therapeutic effect.

With the present crowded curriculum the relief to the student of not having to learn the official posological tables would be welcome. The time wasted in obtaining a fleeting knowledge of official doses for examination purposes could well be devoted to a more thorough understanding of pharmacological actions. Most practising physicians retain a knowledge of doses appertaining only to those drugs which they personally use in practice. They refer to the official list for others. Such a list would still be available under an official unit system.

Traditionalists will object to the delegation of responsibility for dispensing the unit officially adopted to the dispensing chemist. If all preparations were required by statute to be clearly labelled with the amount of the official unit, the dispensing chemist would be in no more responsible position than he is at present with his duty not to dispense beyond the official doses without drawing the attention of the prescribing doctor to any serious overdosage. The D.D.A. list would of course be retained.

The present multiplicity of measures—for example, Imperial and metric systems, volumes, and units—will sooner or later make a unitary system essential. Moreover, an international standard of dosage becomes feasible in a unit system. This we have already in part in the international units in vitamins. Certain drugs may require to be standardized in units of weak and concentrated forms, but this should present no difficulty that cannot be surmounted. New drugs may require to be placed in a transitional category before finally deciding the size of the unit.

This is a plea for realism in prescribing. The adoption of a unit system would do much to simplify the introduction of new drugs which appear, to the confusion of prescribers, under a multiplicity of proprietary names with slight variations in dosage. In these days of rapid advances in therapeutics, any relief in the responsibilities of the practising doctor surely is a desideratum of some priority. Some two years ago this idea of a unit system in prescribing was referred to several industrial concerns for comment. The replies indicated that such a scheme was "unlikely to be very acceptable." The points of objection were chiefly concerned with the changes entailed in textbooks, pharmacopoeias, labels, and promotional literature prepared by the manufacturing houses and, on the dispensing side, the care which would be required in dealing with decimal fractions of a unit, or where the same drug was used for different purposes with different dosage. The latter objection resolves itself into a knowledge of pharmacological actions, and it is not contended that this subject would be made any easier. Indeed, without the obligation to learn the posology of pharmacology, the new graduate would be expected to show a greater understanding of his drugs.—I am, etc.,

BRUCE WILLIAMSON.

London, W.1.

A Journal and Its Readers

SIR,—I agree whole-heartedly with your description (February 28, p. 496) of the *British Medical Journal* as a journal trying to provide "something for everybody." As such it fails, of course, in my opinion to provide very much for anybody—for that is the logical outcome of such an editorial policy. In my rather superficial analysis, the people behind the patient are as follows: (1) The research chemists. Would it be wise to include this work in the *British Medical Journal*? (2) The research biologists (of all kinds). We get little of this in the *British Medical Journal*. (3) The teaching hospital specialists (and the M.R.C.) who juggle with the medical tools produced by groups (1) and (2). I doubt if even they know as much about the materials they use as they might. Surely they are as empirical as any of our predecessors. Summed up, however, the vast majority of this work results in medical "lost causes," an example of this being the current work on the hexamethonium compounds, which is only just holding its own at the present time. (4) The general practitioner and the specialist at the non-teaching hospital.

You quote Clifford Allbutt. The general practitioner applies the science (or whatever amount of science it contains) to the patient. No knowledge of chemistry, biology, or the medical dead-ends of ten thousand years is essential. All that is needed is a wide knowledge of people and the ability to evaluate them and the medical tools at his disposal. The major part of the *Journal* recounts the wrangles of the teaching specialists over non-proven therapeutic methods, each trying to make a name for himself as much as trying to advance medicine, though the unity of these efforts in the long run occurs. The "Refresher Course" (a name insulting to the G.P. and typical of the condescending attitude of Tavistock House), "Any Questions?" (again an insult), and

the leading articles are the only things in the *Journal* of any use to us. "Use" is, of course, the operative word if medicine attempts to be an applied science. The *Practitioner*, on the other hand, treats the G.P. (and the non-teaching specialist) with dignity. It gives the *ex cathedra* treatment for the conditions for which we want to know the science to apply. And it also gives the arguments for such treatments with even, in some cases, the alternative and less successful treatments. It is then up to the individual G.P. to apply such treatment and see whether he can get a better result than he did heretofore.

The more medicine approaches science, the greater the amount of treatment will become formalized and dogmatic rather than the transfer of spirit and personality. Even now, does the writer of a paper on the methonium compounds know so very much more about how those drugs work than the G.P. ?

May I give you the reason for the appearance of the *Medical World* ? It is essential because of the uselessness of the *British Medical Journal* to us "old sticks . . . the applicators of medicine." I do not know the *Lancet* and have not seen enough of the *Medical World* to form an opinion on it. All three of the journals, however, are trying to sort out the successes from the failures of the empirical therapeuticists and present it free from the experimental embellishment.

You say the multiplication of journals for general practitioners ". . . has behind it the assumption that the general practitioner is intellectually inferior to his colleagues. . . ." The assumption is, of course, correct. There is no need to remind us of it. The G.P. is a G.P. because he has neither enough brains nor influence (brains in my case). If I had got a first-class honours degree and knew the right people, do you think I would be seeing sixty to seventy people at my surgeries and twenty calls daily ? When the day is over, one can feel a little tired and unwilling to read wrangles about abstruse medical problems. The capacity of any one human brain is, after all, finite.

If the object of the *British Medical Journal* is both immediately and ultimately to improve the practice of medicine, it should consist of two parts, one part devoted to the evolution of biology and therapeutics, and one part devoted to the nature of disease as it has at the moment of writing been established and the methods of treatment of disease which appear at the moment of writing to be best to the writer.

Until such a reform of your *Journal* is carried out I will continue, as do the vast majority of my fellow G.P.s, to read the summary of each article and the leading articles, with a glance through the parts given over to medical politics. I will, as I always do, read the *Practitioner* from cover to cover. It would be simpler to give my membership of the B.M.A. up and save my six guineas. After all, I can become a founder member of the "College" for ten guineas and have my interests possibly better catered for.—I am, etc.,

Folkestone. J. M. B. MORWOOD.

SIR,—It is difficult to follow your argument in the leading article (February 28, p. 496) under the above heading. You mention that the *B.M.J.* is not a journal for general practitioners, and then deplore the multiplication of journals for general practitioners. The very fact that you claim that the "Refresher Course" series caters especially for the general practitioner shows how little you understand his needs; very few of these articles are of any value to him—they are written by consultants and appear to be based, at best, on hospital out-patient experience.

Your circulation of 78,000 copies does not mean a similar number of readers. Most of us receive the *B.M.J.* free in virtue of our membership of the B.M.A., and all too many copies are never unwrapped. A man is far more likely to read a journal that he has selected and paid for; any excessive multiplication will always be checked by financial considerations.

How can a journal be "what its contributors make it" when all contributions have to pass the scrutiny of one section only of the profession, the consultants ? Certain it is that in 1953 it is easier for a young registrar to have access to your columns with a description of two cases of an extremely rare disease than for a general practitioner "at the peak or over of middle age" to be able to report a discovery similar in value to that of digitalis. We general practitioners need a journal run by men who have shared our experiences and who are "on the same wavelength." We would be the first to resent any suggestion of intellectual inferiority, but already much of "medical science in the making" is not seen by us because of the multiplication of scientific journals that the B.M.A. has found it necessary to sponsor.—I am, etc.,

Bath. CHARLES HAGENBACH.

Chlorophyll as a Deodorant

SIR,—I have read with interest Dr. J. C. Brocklehurst's paper entitled "An Assessment of Chlorophyll as a Deodorant" (March 7, p. 541). I hope that you will publish these comments on it.

Dr. Brocklehurst starts by committing an error, very common in chlorophyll literature, by failing to define his materials. Certainly he makes a show of doing so, but it is meaningless in that he does not give the concentration of any of his samples, except "solution D," which he says is *reported* to contain "12.5% water-soluble chlorophyll." One would want to know the values, based on spectrophotometric assay, in order to assess the worth of his results, as I shall illustrate below. Secondly, Dr. Brocklehurst appears to have discovered an entirely novel, not to say amazing, method for the preparation of methyl mercaptan. Perhaps this accounts for the fact that his product also had novel properties in that 30 mg. had a gaseous volume of 130 ml.—instead of the 14 ml. that one would expect on the usual assumption that a gramme molecule has a volume of 22.4 litres at S.T.P. These aberrations undermine one's confidence in the paper as a whole.

However, assuming that he did in fact have methyl mercaptan, I consider that his first two experiments are valueless, since they failed to comply with the requirement that the water-soluble chlorophyllin and the mercaptan were in intimate contact for a sufficient period of time. Further, since one does not know how much actual chlorophyllin was used in his tests, there is no means of knowing whether the amount of mercaptan was more than could under any circumstances have been deodorized. It is doubtful also whether contact between the chlorophyllin and the odorous materials in his third experiment would have been sufficient, only his fourth experiment being adequate in this respect. Here he fails to define even the amount of mercaptan he used. The failure to deodorize garlic in this case could, from my experience, only arise from the use of insufficient chlorophyllin. Substances such as ether and perfume materials are not deodorized by chlorophyllin under any circumstances.

I have not experimented with methyl mercaptan, but instead have used benzyl mercaptan. If one adds to 100 ml. of water containing 1 g. of sodium copper chlorophyllin (100% by N.N.R. spectrophotometric assay[1]) 0.4 g. of benzyl mercaptan in 2 ml. 90% v/v alcohol and leaves the mixture for 18 hours at 37° C., or at room temperature, it becomes completely deodorized (even if then acidified with sulphuric acid). The green solution now contains a suspension (c. 0.4 g.) of colourless, odourless crystals readily shown to be dibenzyl disulphide, m.p. 71° C. (This approaches the maximum amount of benzyl mercaptan that can be deodorized under these conditions; a smaller quantity is of course much more rapidly deodorized, but contact for an hour or more is still required.) A control experiment at the same alkaline *p*H (9.5), but without the chlorophyllin, reaches a similar result only after about 10 days. Replacement of the air in the vessels by nitrogen results in virtually no change in 21 days or more. Thus it appears that the deodorization of benzyl mercaptan due to aerial oxidation is greatly accelerated by the presence of an appropriate amount of sodium copper chlorophyllin. It is not a catalytic reaction, since the chlorophyllin can deodorize only a limited amount (max. c. 0.5 g.). On recovery, the chlorophyllin shows no apparent change in properties or colour, except that the wavelength of maximum light absorption is altered from 405 μ to 402 μ, but it still will not deodorize any more benzyl mercaptan or, for that matter, any garlic oil.

One might therefore reasonably expect 1 g. of 100% sodium copper chlorophyllin to transform about 0.2 g. of methyl mercaptan to dimethyl disulphide. This latter, unlike the dibenzyl compound, would still have an offensive odour (and incidentally reduce iodine). Whether, being a liquid and perhaps more readily contacted than the very insoluble dibenzyl disulphide, it would react with a further quantity of chlorophyllin to be deo-

dorized (like the diallyl sulphide of garlic oil) remains to be determined. This I propose to try.

Garlic oil differs from benzyl mercaptan in that its main constituent is already a disulphide, the diallyl ester. Here 1 g. of 100% sodium copper chlorophyllin will in 24 hours completely deodorize only about 0.005 g. of the *oil*. Presumably it is again an oxidizing action, but I have not been able so far to identify the product(s). That it is a true deodorization is confirmed by the fact that our parent company now regularly uses sodium copper chlorophyllin to deodorize distillation plant after distilling garlic oil. Such cleaning formerly took 14 days, but is now effected overnight with great saving in expense. Our experiments have revealed that water-soluble chlorophyllins *in vitro* have little or no effect on any substances that we have so far tested, other than odorous sulphur-containing compounds, against which they are highly effective. Since such odorous compounds may often be present in the body as breakdown products of sulphur-containing proteins, it does not seem unreasonable that chlorophyllin should deodorize mouth or breath smells. Systemic deodorization seems less likely. I prefer to leave the clinicians to decide such matters. It is to be remembered, however, that the weight of such materials normally exhaled would presumably be very small indeed as compared with the quantities used in the *in vitro* tests.

I commend Dr. Brocklehurst to try the experiments mentioned above. I shall be very surprised if he fails to confirm my results—that is, assuming that he is using the appropriate chlorophyll derivatives. I shall be happy to supply him with suitable samples on request. Meantime, his present experiments have, in my opinion, proved nothing.

As a mere chemist, I do not feel competent to discuss his clinical results. However, their interpretation may have been biased by the results of his unsatisfactory *in vitro* tests. Further, they constitute only an isolated set of unfavourable subjective results to be set against a much larger number of positive results obtained elsewhere—and must be so regarded.

Finally, while I hold no brief for the wick type of deodorizer, and have already questioned[3] the part chlorophyllin plays in such preparations, I am interested to note the reference in your annotation to the presence of crotonic aldehyde in some of them. What authority exists for this statement? Again, in your references to Dr. A. H. Corwin's criticism, would it not have been fairer also to refer to his subsequent retraction[3] of most of his criticism?—I am, etc.,

WM. MITCHELL,
Chief Chemist,
The Allen Chlorophyll Co. Ltd.

London, N.1.

REFERENCES

1 *J. Amer. med. Ass.*, 1951, **34**, 146.
2 Mitchell, W., *The Export Review*, 1952, **13** (Nov.), 35.
3 *Chemist & Druggist*, 1952, **159**, 238.

SIR,—As a research chemist in the chlorophyll field I feel that a few comments are called for on the article "An Assessment of Chlorophyll as a Deodorant," by Dr. J. C. Brocklehurst (March 7, p. 541) and also on your annotation (March 7, p. 554), especially in view of the subsequent wireless broadcast publicity.

To begin with, under the heading "Chemistry" the formula of chlorophyll is given incorrectly. The magnesium should be directly attached to the nitrogen atoms. After saying that often no information was supplied about the chemical composition of the types of chlorophyll used in proprietary preparations, the author falls into the same error. Admittedly in solution "A" he defines the chlorophyll used, but no indication is given of the purity. Obviously a material testing 60% by the spectrophotometric method would be less effective than a material testing at 120%. Both these strengths are commercially available. In solution "B" one assumes that a crude form of sodium copper chlorophyllin is used, but here again the precise nature of the material is left undefined. Further, the amount of chlorophyll used in preparations described as solution "C" are so small as to be inadequate for the deodorizing experiments subsequently described. Solution "D" again consists of undefined chlorophyll—no information is given concerning the kind or purity.

It is in the experiments, however, that I feel serious criticism can be levelled. In experiments 1 and 2 the time of contact between the mercaptan and the chlorophyll is very short—too short, in fact, for any deodorization to take place, even under the most favourable conditions. For example, work in our laboratories has shown that a period of approximately one hour must elapse for the odour of benzyl mercaptan to be completely removed by sodium copper chlorophyllin at 37° C. Further, the figures obtained are so variable that no reliance can legitimately be placed on them. The number of results reported are totally inadequate having regard to the comparatively crude nature of the experiments. The author admits the magnitude of the experimental error, but we feel his results are practically useless from the point of view of a critical evaluation.

Experiment 3, it is claimed, "involves the use of very much smaller quantities of mercaptan and other odorous vapours," but are the quantities very much smaller? In experiment 1, between 12.6 and 18.5 ml. of 0.1 N iodine solution was reduced, which is equivalent to about 60 and 90 mg. of methyl mercaptan respectively. In experiment 2, 5 ml. of iodine was used, which is equivalent to 24 mg. This compares with 15+30 mg. used in experiment 3. The great weakness of experiment 3, however, is in the author's own admission "that no attempt is made to record the degree of smell present, as the method is too subjective to provide reliable quantitative results." According to the author's technique, even if 90% of the odorous substance were deodorized by the chlorophyll the latter would be classed as ineffective. The Table provided shows that in one case a deodorant effect did occur, but this is dismissed because of the presence of the strong smell of chlorophyll. But surely this would apply equally so to many of the other examples given, particularly the results recorded previously. Comparing these two experiments, it is obvious that, while deodorization had not taken place in 22 hours, it had taken place in 46 hours (even when a smaller amount of chlorophyll was present), and, instead of being dismissed as without significance, it is surely highly significant and should have been made the basis of further experiments.

I am not sure why Dr. Brocklehurst included the experiments with ether, as not only do they bear no relation to the deodorization of breath or body odours, but in any case excessive amounts have been used, running into many hundreds of mg. I do not know the density of methyl mercaptan, but arguing from theoretical considerations—that is, the gramme molecular volume—130 ml. seems to be an excessive volume for 30 mg. of methyl mercaptan. In experiment 4 the results obtained with perfume are quite irrelevant, as it has never been claimed that chlorophyll deodorizes perfume. Further, it is not reasonable to suppose that chlorophyll would penetrate the cell tissue of a slice of onion in sufficient quantity to react with all the odorous substances present. Again no information is given concerning the relative concentrations of chlorophyll and mercaptan used, nor is any definition given of "syrup of garlic."

Finally, the clinical trials described in the paper consist of three people; the first one was given 400 mg. of 10% chlorophyll solution, which means an intake of 40 mg. of chlorophyll of undefined strength daily. From our own experience we know this to be inadequate for this sort of condition. A more likely quantity is 200 to 300 mg. per day of 100% material.

On the subject of the annotation, I should like to point out that the report of the National Bureau of Standards recently quoted by Dr. A. H. Corwin is from section 4, "Control of Odours in Households and Places of Business," subhead 6, "Masking Odours and Their Uses." The subject of the entire circular is space deodorization. The specific reference is to whether chlorophyll can by photosynthesis "purify" enough air to have any distinguishable effect on atmospheric odours. This reference has no application whatsoever to chlorophyll as a *contact* deodorant. As used by Dr. Corwin, this quotation gave the inescapable impression that the National Bureau of Standards had found chlorophyll valueless as a contact deodorant.

In conclusion, may I reiterate that, though chlorophyll is not a panacea for all kinds of odours, work about to be published will show beyond any doubt that in certain specific cases chemical proof is forthcoming that odorous substances can be changed into odourless compounds.—I am, etc.,

L. DEADMAN,
Chief Chemist, Ashe Laboratories, Ltd.

Leatherhead.

SIR,—In the annotation on chlorophyll (March 7, p. 554) reference was made to crotonaldehyde and formaldehyde. We feel sure your readers will be interested to know that neither of these substances is present in "airwick" fluid.—I am, etc.,

B. E. CHANELL,
Managing Director, Airwick, Ltd.

Slough.

Obituary

Mr. M. J. PETTY, senior surgeon at the British Hospital at Buenos Aires, died in that city on January 20 at the age of 64. Michael Joseph Petty was born at Campana, Buenos Aires, on August 27, 1888, the son of the late Dr. Michael John Petty, and in 1896 he was sent to Prior Park School, Bath, where he was a pupil until 1904. Two years later he entered Downing College, Cambridge, graduating B.A. in 1909 and gaining the university scholarship to St. Thomas's Hospital in 1910. He qualified M.R.C.S., L.R.C.P. in 1912, and in 1914 he proceeded to the M.A., took the degrees of M.B., B.Chir., and obtained the F.R.C.S. After qualifying he held house posts at St. Thomas's Hospital and then was resident medical officer at the Lord Mayor Treloar Orthopaedic Hospital for a short time before entering the R.A.M.C. for service in the war of 1914–18. Returning to South America after the war, he received the degree of M.D. of Buenos Aires in 1918 and joined the staff of the Instituto Modelo at the Rawson Hospital, Buenos Aires, in 1919. Two years later he was appointed assistant honorary surgeon to the British Hospital, Buenos Aires, in succession to Mr. J. Wolfe Morris. In 1931 he became senior surgeon of the hospital, an appointment he held until his death. Mr. Petty organized a complete medical and surgical unit to send to the aid of the wounded of H.M.S. *Exeter*, *Ajax*, and *Achilles*, after the Battle of the River Plate in December, 1939. Later in the war he went to the United States to study Professor R. H. Smithwick's operation of sympathectomy for hypertension, and on his return to Buenos Aires he undertook some research on cancer. For his services in the last war he was appointed O.B.E. in 1950. A devout Roman Catholic, Mr. Petty was a past president of the Thomas More Society in Buenos Aires, of which society he was the founder, and at the Eucharistic Congress in 1934 he was the chief organizer of the medical bureau and the first-aid posts. He also founded the Consorcio de Médicos Católicos. An outstanding member of the British community in Buenos Aires, he was associated with its welfare work in many ways, and his loss will be deeply felt by all who knew him. Mr. Petty married Miss Lina M. Pruden in 1920, and she survives him, together with three sons and five daughters.

Dr. E. R. C. COOKE, who practised near Oxford, died at the Radcliffe Infirmary on February 3, after a long illness, at the age of 66. Edward Robert Cecil Cooke was born on June 19, 1886, the elder son of Dr. Edward Cooke, of Sheffield, and was educated at Felsted and Emmanuel College, Cambridge. He continued his clinical studies at University College Hospital and the Sheffield Royal Infirmary, where he held a house post after qualifying in 1913. On the outbreak of war in 1914 he joined the R.A.M.C. and served in France as medical officer to a battalion of the Scottish Rifles, winning the Military Cross in 1917. He later went with the regiment to Palestine. From 1920 to 1933 he was in the Malayan Medical Service, holding many important appointments, including that of chief medical officer in social hygiene. On his return to England he settled in general practice at Little Milton, near Oxford, where he spent the remaining 20 years of his life. In addition to the work of a busy practice he found time to act as honorary secretary to the Oxford Panel Committee, and he was a member of the local emergency committee when war broke out again in 1939. When the Home Guard was formed he served as medical officer to the local battalion. He was also an anaesthetist at the Radcliffe Infirmary and a member of the Oxford County and City Executive Council. In 1951 he suffered a serious illness which necessitated two major operations, but, showing his usual courage during the ordeal, he made a good recovery. He returned to his practice and worked as hard as ever until the end of last year, when he again developed symptoms which called for surgical relief, and his condition slowly deteriorated. Dr. Cooke was a man of fine presence and of great personal charm, and he will be sorely missed by his patients. It was always a great pleasure to visit him at his home, where he and his wife dispensed such charming hospitality. At the funeral service, at which the British Legion formed a guard of honour, the church was filled with his friends and patients from the surrounding district. To Mrs. Cooke and to his son and daughter our sympathy goes out in their great loss.—J. H. C.

Dr. G. C. K. REID, pathologist to the Walsall group of hospitals, died at his home at Walsall on February 6 at the early age of 49. Gordon Campbell Kinloch Reid was born at Elgin on July 9, 1903, and was educated at Perth Academy and at St. Andrews University, where he graduated M.B., Ch.B. in 1929, and also took the diploma of L.D.S. He tried general practice for a time and then returned to hospital work in 1935 as resident surgical officer at New Cross Hospital, Wolverhampton. He devoted himself increasingly to laboratory work until 1938, when he obtained the appointment of resident medical officer and assistant pathologist at the Royal Hospital, Wolverhampton. His clinical experience in general practice and in hospitals helped him to bring together the work of the laboratory and the wards, with mutual benefit. He took a particular interest in the development of the Wolverhampton and District Blood Transfusion Service, which was very much a going concern when the second world war broke out. He joined the R.A.M.C. in 1940 and served with the Eighth Army in North Africa and in Europe, being mentioned in dispatches for conspicuous gallantry and devotion to duty. Released from the Army in 1945, Dr. Reid returned to his work at Wolverhampton until, in 1946, he was appointed assistant and, later, full pathologist at Walsall General Hospital. When the National Health Service came into operation his post as consultant pathologist was widened to embrace the Walsall hospitals group. Late in 1951 illness overtook him and a serious operation became necessary. He returned to duty about a year ago, greatly weakened in strength but full of courage to face the future. Last December he had to undergo a second operation, and, although he left hospital in a cheerful frame of mind, he died in his sleep two days later. His loss is a tragic blow not only to his relatives and friends but also to his patients, who had the greatest cause to appreciate his kindness and his unsparing efforts on their behalf. In 1946 he married Miss Dorothy Pollitt; she brought the skilled experience of a trained nurse to the care of her husband during his many months of illness. Much sympathy will be extended to her and the two children of the marriage.

The first Annual Representative Meeting of the British Medical Association opened in the King's Hall, Swansea, on Tuesday, July 28, 1903, and the jubilee of the Representative Body will be celebrated at Cardiff this year. It is a matter for particular regret, therefore, that the small group of survivors who were present at the first A.R.M. has been still further reduced by the death of Dr. A. TENNYSON SMITH at his home at Bournemouth on February 13 at the age of 82. Alfred Tennyson Smith was born on August 22, 1870, and was educated at the University of Aberdeen, where he graduated M.B., C.M., with honours, in 1892, proceeding to the M.D. in 1898. Dr. Tennyson Smith settled in practice at St. Mary Cray, in Kent, in 1893, and he represented Bromley and Sevenoaks at the A.R.M. in 1903. As a general practitioner, both at St. Mary Cray and later at Orpington, he was greatly loved by his patients and respected by his colleagues. For a number of years he held the appointment of surgeon to the Chislehurst and Cray Valley Hospital. After the first A.R.M. Dr. Tennyson Smith did not represent his constituency again until the London Meeting of 1910, but thenceforward he attended 13 other meetings of the Representative Body until 1932, the year before he retired from practice. From 1914 to 1916 he served on the Central Council of the B.M.A., and from 1921 to 1931

he was a member of the Post Office medical officers subcommittee. He was also honorary secretary of the Bromley Division from 1914 to 1918, chairman in 1922, and president of the Kent Branch in 1923–4. A keen golfer, he presented a cup for annual competition to the Kent Branch of the B.M.A. During the war of 1914–18 he was a major in the R.A.M.C. and was stationed at Port Said for a time. He was keenly interested in the work of the St. John Ambulance Brigade, an interest he maintained after he retired to Bournemouth in 1933. In 1943 he became county commissioner and county vice-president of the Brigade in Hampshire and the Isle of Wight, and in the same year he was appointed O.B.E. for his services to civil defence. Two years later he was created a knight of the Venerable Order of St. John of Jerusalem.

The death occurred in hospital on February 7 of Dr. BALFOUR WILLIAMS at the age of 63. He had been in failing health for some time. Balfour Williams was born in Liverpool on April 4, 1889, and received his medical education at the University of Liverpool, graduating B.Sc. in 1912 and M.B., Ch.B. two years later. From 1914 to 1918 he was surgical tutor and demonstrator at the Royal Infirmary, Liverpool, afterwards becoming resident medical officer at the Liverpool Open-air Hospital, Leasowe, where he remained for some years. Then followed ten years as senior resident medical officer at Mill Road Infirmary, Liverpool. Dr. Balfour Williams was a prominent freemason and was a past master of the University Lodge at Liverpool and of the Birkenhead Hamilton Lodge, of which he was also a founder member. He was also a past provincial grand deacon for Cheshire. Dr. Balfour Williams was a kindly man, quietly but deeply religious. Many Liverpool students during the years 1914–18 will remember him with great affection as an enthusiastic and energetic teacher. He had been in practice at Upton, near Birkenhead, for only a few years, but he had already endeared himself to his many patients. The sincere sympathy of his colleagues, his numerous former students, and his patients will be extended to his widow.—H. C. W. B.

We record with regret the death of Dr. H. G. THOMPSON at Ashford Hospital, Kent, on February 13 at the age of 73. Hubert Gordon Thompson was born at Liverpool on February 24, 1879, the son of Mr. J. Albert Thompson, and was educated at University College, Liverpool, graduating M.B., Ch.B. at the Victoria University of Manchester in 1903. He then held a number of appointments at Liverpool University, being Holt Fellow in physiology and pathology in 1903–4, Robert Gee Fellow in human anatomy in 1904–5, and assistant lecturer in anatomy in 1905–6. After taking the Liverpool M.D. in 1906 he went to stay with his missionary friend, Dr. Neville Bradley, at Pakhoi, in South China, and on his return to this country he took the F.R.C.S. and offered his services as a medical missionary to the Church Missionary Society. After working for a time at the Pakhoi Hospital and leper settlement he paid several visits to the distant province of Yunnan, and in 1917 opened up a C.M.S. hospital at Yunnan Fu (now known as Kunming). Within two years the Chinese Government awarded him a special civil decoration in recognition of his services. After the resignation of Dr. D. Duncan Main from the post of medical superintendent of the unique C.M.S. agglomeration of hospitals and medical institutions at Hangchow, he was called to take charge of those institutions in 1926, at a time when the Nationalist disturbances were a sore trial to China. Two years later he resigned from the C.M.S. on his appointment to the chair of surgery at the Henry Lester Institute of Medical Research in Shanghai. It says something for the spirit of the man that, when some years later a serious need for staff arose at one of the C.M.S. hospitals in the far west of China, Gordon Thompson, though aged 70, offered to return temporarily to meet that need. He was a good administrator, a tactful leader of men, and a man of great personal charm and religious faith. His physical endurance was remarkable, and, with General Pereira, he made an epic journey of exploration through the borderlands of Tibet about 30 years ago. His home at Kunming gave him the opportunity to entertain many distinguished explorers and scientists, such as Captain Kingdon Ward, Dr. Rock, and others. He married Miss Amy Bradley, the sister of his friend and colleague, in 1912, and his daughter, Dr. Greta C. Hague, has returned with her husband to the mission in South China to which her father first went nearly 50 years ago.—H. G. A.

We record with regret the death of Dr. RALPH NORMAN at his home at Thorpe Bay, Essex, on February 21 at the age of 77. Ralph Norman was born on December 15, 1875, and was educated at Epsom College and at the London Hospital, qualifying M.R.C.S., L.R.C.P. in 1899. He graduated M.B. from the University of London in 1903, proceeding to the M.D. in the following year. After qualification he held the appointments of paediatric house-physician and resident obstetrician at the London Hospital, and later became deputy medical superintendent of St. Andrew's Hospital for Nervous and Mental Disorders, Northampton. In 1907 he joined Dr. Charles Forsyth in practice at Southend-on-Sea, where he rapidly established a reputation for sound clinical judgment and versatility. He was assistant physician to the former Southend-on-Sea Victoria Hospital, and later assistant physician to the new Southend General Hospital. For some years he was consultant physician to Rochford Hospital, where the staff were grateful for his opinion and help over an extensive field, including difficult midwifery. During the war of 1914–18 he rendered valuable service as physician to the Queen Mary's Hospital, Southend-on-Sea, and was a member of a medical board. From 1928 to 1931 Dr. Norman was chairman of the South Essex Division of the B.M.A.

We are indebted to Dr. J. STEVENSON LOGAN, medical officer of health for the County Borough of Southend-on-Sea, for the following appreciation: The colleagues of Ralph Norman soon came to recognize his gifts and judgment, for in the days when specialists were not as readily available as they are to-day he was often called into consultation by other practitioners, many of whose wives he attended at their confinements. He was associated with the work of the local authority as medical officer at the infant welfare centres and antenatal clinics from the earliest days of the work, and even after his retirement from active practice he remained faithful to his infants clinic until his last illness. During the last war he was a source of strength to the local medical war committee, and he served also as a member of the local obstetric committee and on a medical board. In his young days he played lawn tennis for Essex, and he helped to found the Southend-on-Sea Doctors' Cricket Club, which still flourishes. At the bridge table he was brilliant and formidable. Norman was a very modest man who avoided controversy and never criticized others. He had strong convictions, which he never obtruded, and seemed to know instinctively and without self-questioning which was the right course of conduct; to that he held unfalteringly. He never wasted time and could be brusque with those who tried to waste it for him. Completely honest, always forthright, generous, helpful, and courageous, he was greatly liked by those to whom he accorded the privilege of his friendship. Not the least engaging of his qualities was his quiet, pervasive sense of humour and a genuine love of fun. He loved small children, and was very successful in dealing with them. In his home life he was greatly blessed, and the serenity of the companionship between him and his wife impressed all their friends. He is survived by Mrs. Norman, by their son, who succeeded him in his practice, and by a daughter.

We are indebted to Dr. T. M. LING for the following appreciation of Dr. HAROLD BALME, whose death was recorded in the *Journal* of February 28 (p. 511): The outstanding memory that his colleagues have of Harold Balme is of his enthusiasm, activated by a strong Christian spirit. His work as professor of surgery at Cheeloo University at Tsinan

in China gave him a wide circle of friends in the Far East. In more recent years his work in the field of rehabilitation gave him another circle of friends, who were equally stirred by his passionate enthusiasm and eloquence. In the war years he laid the foundations of hospital rehabilitation facilities up and down the country, being far-sighted enough to use the war situation to help the whole civilian population. Balme was always rather an impatient man and did not hesitate at times to criticize to good effect the bureaucratic machine and those who worked it. There is no doubt that the hospital rehabilitation departments that he created were pioneer ventures that have proved their worth. The development of physical medicine in this country owes a bigger debt to Balme than is always realized.

Since the second world war Balme devoted all his energies to international medicine, serving in the joint post of adviser on rehabilitation to the United Nations, the World Health Organization, and Unicef. This position called for considerable tact, and in addition Balme displayed his customary zeal. He was largely responsible for the excellent rehabilitation centre near Graz in Austria that has proved an inspiration to many visitors from central Europe. Throughout these latter years Balme was chairman of the Working Party on Rehabilitation, which acted as a liaison between the United Nations and all the specialized agencies. Balme's contributions were recognized as showing great vision, and he was always anxious to bring modern rehabilitation techniques to less-developed countries.

For the last year Balme suffered from increasing ill-health, but he had great fortitude, and his keenness was never impaired. During his final months he passed on many fresh ideas to the younger generation, and one of his great regrets was his inability to attend the Working Party meeting at the United Nations this winter. Balme will be sadly missed by his many friends; his practical idealism was all too rare in this materialistic age.

Medical Notes in Parliament

CONTROL OF HOSPITAL FINANCE

Different aspects of National Health Service administration were discussed in the House of Lords on March 4, when LORD AMULREE called attention to the difficulties imposed on hospital committees by the implied rigidity of recent instructions from the Ministry of Health, and LORD SALTOUN complained of the rigid application of the drug tariff to the prescribing of appliances.

LORD AMULREE said there was increasing anxiety among hospital staffs and management committees, and among the governors of teaching hospitals, that the Ministry of Health was showing a desire to control more and more the day-to-day running of hospitals, and particularly the staff appointments, both medical and lay. Two circulars recently issued had shown great interest in the size and control of hospital staffs, and were contrary to a promise when the National Health Service Bill was going through Parliament that each hospital would be free to decide within the limits of its budget how its money should be spent.

The first request for information about medical staffs came in February, 1951. It was followed by another, for very detailed information about the consultants, their names, the hours they worked, what people they had working under them, and so forth. For the hospital at which he worked it entailed a return of 29 foolscap pages, and he did not think it would be of great value when it was received. That was followed by a medical survey. Teams were sent round the hospitals to review staff and make recommendations on the appropriate staffing, which it was intended should become "frozen" in December 6 last. Before that occurred, however, there was another demand for information on staffing in September, 1952. From this it appeared that the boards would be able to increase the approved medical establishment in any grade only with the Minister's consent. There had since been some substantial modifications in that, but there was great trouble and confusion, between the issue of the circular and the final modification, which was issued only the other day.

There had also been a further circular entitled "Economy in Manpower," dated December 5, 1952, requiring returns within 14 days of medical and administrative staffs. Survey teams visited the hospitals again, and made inquiries and recommendations. From the kind of things that occurred it was difficult to believe that this was not centralized control coming along. Hospitals should be allowed to do their work without interference from some central controlling organization. They were very much tied up from the point of view of salaries. Everything was fixed. Limits were laid down by the central authority. Why should not people be allowed, if they had a budget of sufficient size, to pay out sums, including salaries, which they thought reasonable and appropriate?

Rigidity of Drug Tariff

LORD SALTOUN'S point was that rigidity should be relaxed to permit the use of appliances not less efficient nor more expensive than those of the kind listed in the drug tariff. The circumstances in which it originated, he said, were that a doctor prescribed for an N.H.S. patient two tins of "penicillin nonad tulle" dressings, 2 in. square. The two boxes contained 72 dressings and cost 10s. 6d. In due course the prescription went to the executive committee, who refused to repay the chemist because these dressings were not appliances coming within the Third Schedule to the General Medical and Pharmaceutical Services Regulations. In fact, this dressing was included in the drug tariff, but only in sizes of 4 in. square, and the cost was 5s. for a tin of 10, or 36s. for the 72 ordered by the doctor. Presumably the prescribing doctor thought the nature and position of the wound required the smaller dressing. The chemist was compelled to fulfil the order. Together they had incurred for the Service a charge of 10s. 6d. and avoided one of 36s. Yet all that happened was that the chemist was refused payment. This was not a solitary case. He had a long list of other examples. There should be some relaxation of rigidity; or alternatively they might adopt the Scottish system, in which the majority of appliances in the drug tariff were listed in the most generalized form.

New Scheme Devised

The EARL OF ONSLOW, speaking for the Government, replied first to Lord Saltoun, and said that after making extensive inquiries about the drug tariff he believed that it was almost 99% foolproof. In a few weeks a scheme would be devised with a small enough mesh to catch the anomalies. The particular item Lord Saltoun had complained of was not in the tariff because it was considered that that size and quantity of penicillin dressing was so rarely used in general practice that its inclusion might lead to waste.

The first of the two documents quoted by Lord Amulree (B.G. 4/72/201) was not a circular but a letter written to teaching hospitals. Medical review teams had studied the staffing of the hospitals, and made suggestions to the Minister. The letter brought these suggestions to the notice of the teaching hospitals and asked for their views, and was by no means an order to the hospitals to alter their day-to-day arrangements. The other document that had been quoted was a circular, but again it was not an order; if the hospitals found that they could not comply with the suggestions put forward in it they were entitled to say so. The main intention was to keep a check on proposals for increases of staff, particularly administrative and clerical. The review on which it was based was started as long ago as 1950, and one aim was to produce an eventual reduction of something like 5% on the clerical and administrative side. But again these were not orders, merely suggestions. It was part of the scheme to pool information and resources in order to keep down cost; and there was no wish, he emphasized, to interfere on the medical side.

Too Detailed Direction

LORD KENSWOOD said that the Ministry of Health must lay down the general lines about how the money allotted to the management committees and boards of governors should be used, but the difficulty arose because the direction had been made too detailed and rigid. That removed the initiative, enthusiasm, and imagination from the voluntary workers. The management committees and regional boards should be given much more elbow room, so that money saved in one direction could be used in another. In the end that would be good business and good economy.

LORD LUKE assured the Minister that those who were responsible for watching hospital finances were doing their best to carry out the economies asked for, although it was difficult because so much of their expenses was outside their control.

LORD BURDEN suggested that even to maintain the standards of hospital services of two years ago would be impossible, in view of rising prices and increased rates of payment, without increased Exchequer grants. On the Government's present policy there could only be lower standards of service. He referred to the "stupid rigidity" of the circular, and the EARL OF ONSLOW interrupted: "If a hospital feels it is running as economically as it can there can be no question of asking it to reduce expenditure in any way."

Government Reply

The LORD CHANCELLOR, replying to the debate, pointed out that the Minister of Health was faced with the eternal conflict between a proper supervision of national finances and the requisite delegation of authority. He had also to see that there were fair shares for all. Equality of conditions should be observed as far as possible. The overriding consideration was that the Minister was responsible for the money spent, and when it was realized that for hospital services alone the Health Service was now demanding annually a sum approaching £300m. it would be realized how essential it was that supervision should be strict—he would avoid the word "rigid."

The circular on staffing left a considerable amount of flexibility within the various categories. There was not to be a total increase of staff without the Minister's consent, but there was no reason to suppose that, if a proper case was made, consent would not be forthcoming. The circular recognized that increases might be made, and indeed suggested that they ought to be made, in some mental and tuberculosis institutions.

Reverting to Lord Saltoun's complaint, he said that a doctor should be aware of what were the things he was entitled to order, and if he chose to order something not on the list he ran a grave risk in so doing.

Problem of Aged Sick

The House of Commons on March 6 agreed to a motion presented by Mr. BARNETT JANNER expressing concern at the shortage of hospital beds for the chronic and aged sick, and the lack of accommodation for those who needed care and attention rather than medical treatment. He urged the Government and hospital authorities to hasten the establishment of a comprehensive geriatric service to cover the whole country.

Mr. K. ROBINSON, seconding the motion, said the aim was to emphasize the rehabilitation of the patient. There should be a properly integrated geriatric unit in every hospital above, say, 500 beds.

Mr. SOMERVILLE HASTINGS said the problem would not be solved until there was in every locality one authority for health and welfare functions, so that the care of the aged, whether ill or well, would be a continuous process by one authority.

Dr. EDITH SUMMERSKILL said it was estimated that by 1975 there would be 8½ million people over 65, compared with the 5 million to-day. Proper diagnosis of chronic sickness in hospitals, followed by the proper treatment of the old people at home, with the help of out-patient geriatric services and discretionary allowances from the National Assistance Board, could change the whole outlook of these aged patients and their families. The provision of one hot meal a day and a fully staffed district nursing service was most important. 60% of the work of district nurses was concerned with elderly people, and because of overwork they were being forced in some places to cut down their visits. To approach the problem in an economic way meant ensuring a well-staffed district nursing service.

Miss PAT HORNSBY-SMITH accepted the motion on behalf of the Government. She described the problem of the aged and chronic sick as the biggest challenge to the welfare State. The cost of retirement pensions, which were expected to total £420m. in 1958, was estimated to increase to £700m. in 1978. There were 82,000 more people over 65 in mid-1952 than in mid-1951. Hospital management committees and local authorities were doing their best to meet the problem, but it was growing faster than the facilities to deal with it. While the number of beds in use for chronic sick patients rose by 1,700 (or just over 3%) in 1951, the number of patients rose from 83,852 to 93,390. Figures available for 1952 showed an increase of 1½% in the number of patients treated. The Government recognized the problem, but it could not be solved by the State alone. The co-operation of the community, the voluntary organizations, and the family was needed.

Analgesia in Childbirth

Miss JENNIE LEE asked on March 5 what was the percentage of mothers who were given analgesia among those whose children were born at home; and the percentage given any other treatment to relieve pain of a kind that required special equipment and special training on the part of midwives.

Miss PAT HORNSBY-SMITH replied that of the mothers attended by midwives in their homes in 1951, the latest year for which figures were available, 58% had gas-and-air analgesia; 25% of the mothers were given pethidine.

Mr. SOMERVILLE HASTINGS asked if he was right in assuming that in many areas all midwives had been trained in giving analgesia, and that in most areas a large percentage were thus trained. Miss HORNSBY-SMITH said that was quite right. The overall figure was 90%, and in many areas it was 100%.

Composition of Flour

Dr. CHARLES HILL on March 2 supplied Mr. H. HYND with the following details of the chemical composition of representative flours:

Nutrients per 100 g.	Extraction Rate		
	80% National (including Added Calcium Carbonate)	70–72% (Unrestored)	70–72% (Restored) (including Added Calcium Carbonate)
Energy value (calories) ..	341·0	343·0	343·0
Carbohydrate (g.) ..	70·2	72·0	72·0
Protein (g.)	11·7	11·3	11·3
Fat (g.)	1·4	1·1	1·1
Calcium (mg.)	143·0	16·0	142·0
Iron (mg.)	1·65	1·25	1·65
Vitamin B_1 (mg.) ..	0·24	0·08	0·24
Nicotinic acid (mg.) ..	1·6	0·8	1·6
Riboflavin (mg.) .	0·06	0·05	0·05

Overcrowding in Prisons

A debate on conditions in prisons, initiated by Mr. V. F. YATES on March 2, was concerned largely with overcrowding. He spoke of the increasing number of prisoners—over 5,500—who slept three in a cell; and of a visit with members of the Select Committee on Estimates to Wandsworth, where he was shocked and horrified by what he saw. Dr. Murdoch, the principal medical officer of Wandsworth Gaol, had stated in evidence about overcrowding: "It can only be condemned by any doctor"; and later..

"I cannot imagine any dwelling-house with one closet to 40 people. It is a disgusting thing. On the question of epidemic disease, if one man gets a disease the others will get it." It was contrary to all principles of humanity and justice, Mr. Yates said, that in addition to sentence a prisoner should be thrown into conditions which were a grave danger to health.

Sir DAVID MAXWELL FYFE, Home Secretary, acknowledged the extent of overcrowding, but pointed out that a total of 24,000 persons in prison had not been known in this country for 70 years. This sensational increase was confined to male prisoners, and the overcrowding to which it gave rise was concentrated in the local prisons. There were 5,680 men prisoners sleeping three in a cell, a state of affairs that nothing but necessity could excuse. So far there seemed to have been no epidemics, and there seemed to have been no effect on health and hygiene at all.

Food Consumption

Major LLOYD-GEORGE informed Mr. F. T. Willey on March 4 that the average civilian food consumption was 3,000 calories per head per day before the war, against 2,950 in 1952. The comparable animal protein figures were 43.2 g. and 42.0 g.

Margarine Content

Mr. PETER FREEMAN wanted to know the proportion and content of each ingredient in each variety of margarine. Dr. CHARLES HILL informed him on March 2 that the main variety, known as "special" margarine, contained hard and soft vegetable oils and marine oils in proportions which were frequently varied according to the supply and the time of year, as well as milk, salt, flavouring, and vitamin. The only other variety on sale to the public was kosher and vegetarian margarine, which contained no marine oil, milk, salt, or flavouring.

Therapeutic Substances Bill

The Therapeutic Substances (Prevention of Misuse) Bill was read a third time in the House of Lords on March 3, and sent to the Commons.

Cortisone Production.—Mr. Iain Macleod stated on March 5 that production of cortisone in this country had started, but output was not yet sufficient to meet current needs. Distribution was restricted to selected hospitals, and he hoped gradually to increase the quantities issued.

The Services

DOMVILLE MEMORIAL GIFT

The trustees of the Domville Memorial Gift wish to elect a recipient on or about March 14. The present value is £5 7s. 8d. yearly, tenable for three years. The recipient must be a child (or children) of a deceased Naval medical officer, and in necessitous circumstances, and under the age of 15 years. Particulars of claim and birth certificate(s) should be forwarded by March 10 to the honorary secretary, Domville Memorial Gift, R.N. Hospital, Haslar, Gosport, Hants, who will give any further information desired.

Surgeon Lieutenant-Commanders A. R. Harper, G. Hayes, and A. B. Semple, R.N.V.R., have been awarded the R.N.V.R. decoration.

Major-General E. P. N. Creagh, late R.A.M.C., has been appointed Honorary Physician to the Queen in succession to Major-General T. Menzies, C.B., O.B.E., late R.A.M.C.

Brigadier R. Murphy, C.B.E., late R.A.M.C., has been appointed Honorary Surgeon to the Queen in succession to Major-General R. D. Cameron, C.B., C.B.E., M.C., late R.A.M.C., retired. He has also been appointed a Deputy Director of Medical Services of the Army, and has been granted the temporary rank of Major-General.

Brigadier F. C. Hilton-Sergeant, late R.A.M.C., has been appointed a Deputy Director of Medical Services of the Army, and has been granted the temporary rank of Major-General.

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending February 21 (No. 7) and corresponding week 1952.

Figures of *cases* are for the countries shown and London administrative county. Figures of *deaths* and *births* are for the 160 great towns in England and Wales (London included), London administrative county, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES in Countries and London	1953 Eng. & Wales	1953 Lond.	1953 Scot.	1953 N. Ire.	1953 Eire	1952 Eng. & Wales	1952 Lond.	1952 Scot.	1952 N. Ire.	1952 Eire
Diphtheria	16	2	19	0	4	37	3	21	1	1
Dysentery	241	29	136	10		591	56	78	3	1
Encephalitis, acute	8	0	1	0		5	0	0	0	
Enteric fever:										
Typhoid	8	0	1	0		3	0	0	1	3
Paratyphoid	4	0	7(B)	0		6	0	1(B)	0	
Food-poisoning	194	23		0		85	21		0	
Infective enteritis or diarrhoea under 2 years				5	22				10	13
Measles*	32,890	1832	447	119	399	5,734	123	483	152	137
Meningococcal infection	63	8	28	7	2	45	5	25	3	5
Ophthalmia neonatorum	44	1	8	0		40	2	13	1	
Pneumonia†	2,142	117	475	30	17	1,143	50	478	20	3
Poliomyelitis, acute:										
Paralytic	25	3	2	0	2	9	1	1	1	
Non-paralytic	2	0				5	0			
Puerperal fever§	258	33	8	4	1	218	39	9	2	
Scarlet fever	1,550	83	264	39	73	1,613	141	251	18	55
Tuberculosis:										
Respiratory			158	29				161	29	
Non-respiratory			28	4				35	4	
Whooping-cough	2,197	121	253	29	126	2,648	128	418	103	73

DEATHS in Great Towns	1953 Eng. & Wales	1953 Lond.	1953 Scot.	1953 N. Ire.	1953 Eire	1952 Eng. & Wales	1952 Lond.	1952 Scot.	1952 N. Ire.	1952 Eire
Diphtheria	0	0	0	0	0	0	0		0	0
Dysentery	0	0		0		0	0		0	
Encephalitis, acute		0			0		0			0
Enteric fever	0	0	0	0		0	0		0	
Infective enteritis or diarrhoea under 2 years	9	4	1	1	2	14		1	0	1
Influenza	521	79	27	2	4	29	6	9	1	0
Measles		0	0	1	1		0	1	0	0
Meningococcal infection		4	0				0			
Pneumonia	772	109	40	10	17	368	57		18	20
Poliomyelitis, acute	3	0			0	0	0			0
Scarlet fever		0	0	0	0		0		0	0
Tuberculosis:										
Respiratory	151	24	34	5	7	176	24	30	4	14
Non-respiratory		2	0	1	3		3	5	1	4
Whooping-cough	9	0	0	0	0	4	0		2	1
Deaths 0–1 year	316	41	36	10	17	296	32	43	23	13
Deaths (excluding stillbirths)	9,038	1345	808	128	206	6,856	967	796	162	202
LIVE BIRTHS	8,047	1179	925	217	335	8,101	1249	910	234	375
STILLBIRTHS	190	20	23			231	30	28		

* Measles not notifiable in Scotland, whence returns are approximate.
† Includes primary and influenzal pneumonia
§ Includes puerperal pyrexia.

Vital Statistics

Scotland's Health in 1952

The death rate from tuberculosis continued to improve greatly. It was 32 per 100,000 population, which is 11 below the rate for 1951, and 32 below the average for 1947–51. The rate for pulmonary tuberculosis was 27 and for non-pulmonary forms 4 per 100,000. Glasgow showed a higher tuberculosis mortality rate than other cities—55 per 100,000 compared with 30 in Edinburgh, 22 in Aberdeen, and 25 in Dundee.

The infant mortality rate of 35 per 1,000 live births was the lowest ever recorded in Scotland, and was 2 below the rate for 1951. Again Glasgow had the highest rate of the cities at 41 per 1,000. Edinburgh was lowest with 29, and Aberdeen and Dundee were 30 and 31 respectively.

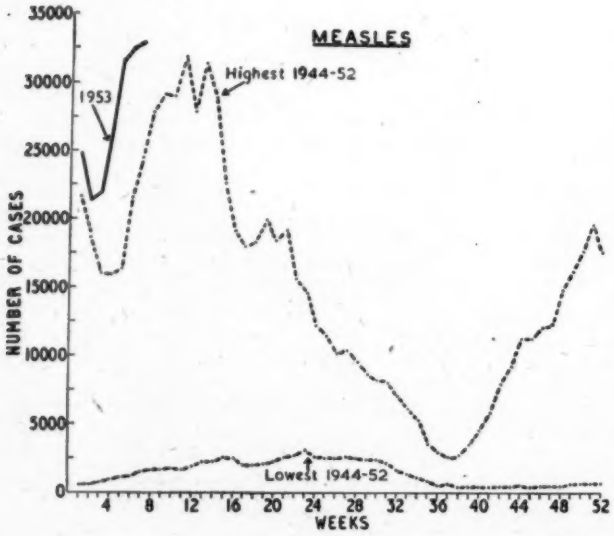
Edinburgh had the oldest and Glasgow the youngest populations, with Aberdeen and Dundee standing between, rather nearer to Edinburgh. Partly no doubt because of this, Glasgow had the highest birth rate at 18.7 per 1,000 population and Edinburgh the lowest at 15. The birth rate for Scotland as a whole was 17.7 per 1,000 population, the same as for 1951, and 1.4 below the average rate for 1947–51. Births outnumbered deaths by about 29,000, but migration into and out of Scotland resulted in a loss of some 24,000 people, so there was a final increase in population of between 4,000 and 5,000: it was estimated to be just over 5 million at the end of the year. (Preliminary figures issued by the Registrar-General for Scotland.)

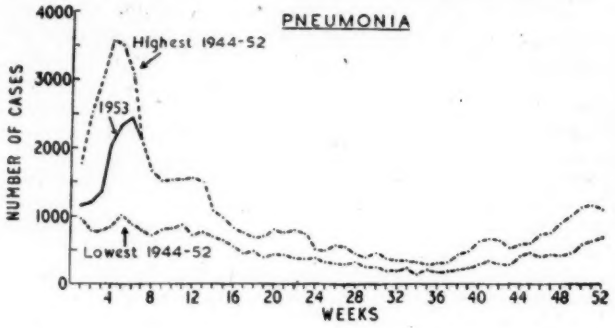
Week Ending February 28

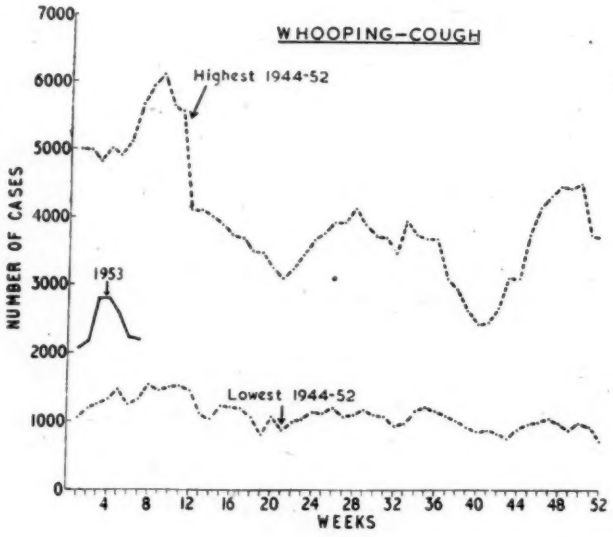
The notifications of infectious diseases in England and Wales during the week included scarlet fever 1,455, whooping-cough 2,746, diphtheria 27, measles 30,884, acute poliomyelitis 13, dysentery 252, paratyphoid fever 2, and typhoid fever 4.

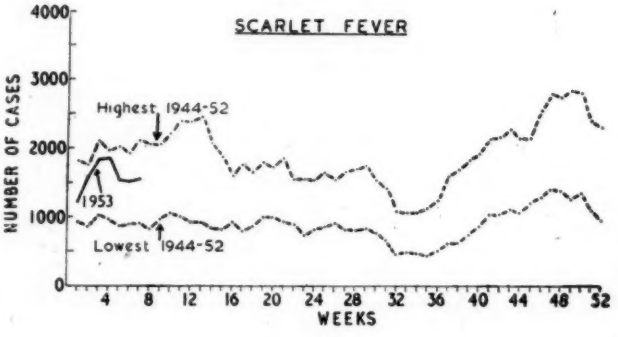
Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of certain diseases notified weekly in England and Wales. Highest and lowest figures reported in each week during the nine years 1944–52 are shown thus - - - - - - - -, the figures for 1953 thus ————. Except for the curves showing notifications in 1953, the graphs were prepared at the Department of Medical Statistics and Epidemiology, London School of Hygiene and Tropical Medicine.









Infectious Diseases

The only large fluctuations in the incidence of infectious diseases in England and Wales during the week ending February 21 were an increase of 531 in the number of notifications of measles, from 32,359 to 32,890, and decreases of 289 for pneumonia, from 2,431 to 2,142, and 79 for dysentery, from 320 to 241.

The largest rises in the incidence of measles were 370 in Surrey, from 1,486 to 1,856; 325 in London, from 1,507 to 1,832; 302 in Yorkshire West Riding, from 1,867 to 2,169; and the largest falls were 556 in Southampton county, from 2,187 to 1,631; and 298 in Devonshire, from 1,139 to 841. The notifications of scarlet fever, 1,550, were 35 more than in the preceding week, and with the exception of a rise of 35 in Lancashire, from 225 to 260, only small variations were recorded in the local trends. Notifications of whooping-cough decreased from 2,238 to 2,197; the largest fluctuations in the local returns were an increase of 28 in Durham, from 72 to 100, and a decrease of 45 in Kent, from 94 to 49. 16 cases of diphtheria were notified, 8 fewer than in the preceding week. The chief feature of the returns of diphtheria was a fall in Lancashire from 9 to 2.

Of the 8 cases of typhoid fever, 5 were notified in Yorkshire East Riding, Haltemprice U.D.

Notifications of acute poliomyelitis were 10 more for paralytic cases (25) and the same for non-paralytic cases (2) as in the previous week. The largest returns were Warwickshire 4 (Birmingham C.B. 4), Lancashire 3, London 3 (Wandsworth 2), and Yorkshire West Riding 3.

The chief centres of dysentery were Lancashire 63 (Liverpool C.B. 42, Manchester C.B. 12), London 29 (Stepney 6), Lincolnshire 29 (Grimsby C.B. 22), Yorkshire West Riding 27 (Leeds C.B. 9).

Influenza

Influenza deaths in the great towns of England and Wales showed in the week ending February 28 a sharp fall to 314 from 521. About half of this decline was in the London area; the other half was spread fairly evenly over the North of England, in the regions where in the preceding week there had been a slight increase in deaths from influenza.

Medical News

Medical Society of London.—The 173rd anniversary dinner of the Medical Society of London was held at Claridge's on March 5, with Dr. Cuthbert Dukes, the president, in the chair. In proposing the health of the Society Sir Harold Nicolson paid a handsome tribute to its founder Lettsom, and to his biographer, Dr. Johnston Abraham. Lettsom, he said, was a man who believed intensely in the profession to which he belonged. It was recorded that he used to see 50 poor patients before breakfast. Lettsom said that he early acquired the habit of being kind to his patients—by no means a usual habit in those days. Sir Harold concluded an entertaining speech by asking his audience to treat "literary neurotics" with care. In response Dr. Dukes said the Society was in a robust state of health, and that this was in no small part due to the devoted and loyal service of the council of the Society and their two secretaries, Dr. A. L. Wingfield and Mr. Nils Eckhoff. During the year the Society had received gifts of pictures, books, and microscopes. The health of the visitors was proposed by Dr. Cochrane Shanks, and Dr. F. M. R. Walshe replied.

Fund for Poliomyelitis Research.—Sir Russell Brain, P.R.C.P., and the Minister of Health, Mr. Iain Macleod, were among the speakers at last week's dinner at the Mansion House in aid of the National Fund for Poliomyelitis Research. The Lord Mayor of London presided. The Fund has been launched by a lay organization of sufferers from the disease, the Infantile Paralysis Fellowship. A sum of £2,560 was raised at the dinner.

Stage Hypnotism.—The London County Council has now decided to ban stage hypnotism in London from January 1 next year. This year written consent from the L.C.C. is required (see *Journal*, November 29, 1952, p. 1215). Local authorities have powers to regulate or prohibit exhibitions of hypnotism under the Hypnotism Act, 1952, which comes into force on April 1.

Swiney Prize.—This prize is awarded every five years by the Royal Society of Arts to the author of the best published work on jurisprudence. The prize is offered alternately for medical and general jurisprudence, but if there is no work of sufficient merit in the class whose turn it is to receive the award the prize may be given to the author of a book in the other class. This time it is the turn of general jurisprudence. The prize is a cup of the value of £100 and money to the same amount. Entries should be sent to the secretary, Royal Society of Arts, John Adam Street, Adelphi, London, W.C.2, not later than November 30.

Exhibition of Medical Periodicals.—There will be an exhibition of the current medical periodicals of the world at B.M.A. House next July, in connexion with the first International Congress on Medical Librarianship. Editors and publishers not at present exchanging their journals with any of the publications of the British Medical Association are invited to send copies for display at the exhibition. The journals should be addressed to the information officer, *British Medical Journal*, B.M.A. House, Tavistock Square, London, W.C.1, and marked "Exhibition."

First International Congress of Neuropathology.—The transactions of this congress (which took place in Rome from September 8 to 13, 1952) are shortly to be published. They will comprise two volumes of about 500 pages each, and over 500 illustrations. Further particulars may be obtained from Dr. A. Ferraro, 722, West 168th Street, New York, 32.

Change of Address.—The plastic and jaw unit at Hill End Hospital, St. Albans, is moving to Mount Vernon Hospital, Northwood, Middlesex, on March 16. The unit will be known as the "Mount Vernon Centre for Plastic Surgery and Jaw Injuries." Telephone No.: Northwood 1234, extension 51.

Dr. B. R. Nisbet, medical officer of health for Kilmarnock, has been awarded a World Health Organization travelling fellowship to study public health administration in the United States and Canada. He leaves this month for a two-months tour.

Dr. F. L. Spalding, honorary gynaecologist to the Worcester Royal Infirmary, has been nominated Mayor of Worcester for Coronation year. He is the city's senior alderman, and his connexion with the Royal Infirmary dates from 1899, when at the age of 13 he joined the dispensing staff. He qualified in 1914.

Emergency Bed Service: Applications and Admissions.—During the seven days ending March 9 the number of applications made by doctors to the London Emergency Bed Service for admission of patients was 1,433, of whom 87.98% were admitted.

COMING EVENTS

Oxford and Cambridge Boat Race.—Messrs. Vitamins Limited announce that they have available a limited number of tickets for doctors who may wish to view the Boat Race on March 28 from the Bemax premises. Early application should be made to Dept. B.R.2, Vitamins Limited, Upper Mall, London, W.6.

Developments in Microscopical Methods.—A symposium and exhibition on developments in microscopical methods is to be held by the Royal Microscopical Society (in collaboration with the Institute of Physics, the Physical Society, and the Society of Public Analysts and other Analytical Chemists) at King's College, Strand, London, W.C.2, on March 20. The symposium will be opened by Professor J. T. Randall, F.R.S., at 2.20 p.m.

Faculty of Radiologists.—A postgraduate week-end course will be held by the Faculty of Radiologists at the Royal College of Surgeons on March 21 and 22. Full particulars may be obtained from the Faculty's offices at 45, Lincoln's Inn Fields, London, W.C.2.

Contraceptive Technique.—A lecture-demonstration on contraceptive technique will be given by Dr. Marie Stopes at the Mothers' Clinic, 108, Whitfield Street, London, W.1, on April 2 at 2.30 p.m. No fee is charged, but tickets must be obtained in advance, as space is very limited.

Medical Photography Exhibition.—As part of its centenary celebrations the Royal Photographic Society has planned an exhibition to demonstrate the growth of photography in medicine. This show will be held from April 7 to 30 at the house of the Royal Photographic Society, 16, Princes Gate, London, S.W.7. It will be open from 9.30 a.m. to 5.30 p.m. during the week (5 p.m. on Saturdays), and admission is free.

The Tuberculosis Educational Institute (N.A.P.T. and Joint Tuberculosis Council) has organized a refresher course for doctors on "Radiology in the Treatment of Tuberculosis," to be held at St. Thomas's Hospital Medical School, London, S.E.1, from April 14 to 17. The fee for the course is £4 4s., and tickets are obtainable from the secretary of the Institute, Tavistock House North, Tavistock Square, London, W.C.1.

European Association against Poliomyelitis.—The next General Statutory Assembly of the European Association against Poliomyelitis will be held at the State Institute of Serotherapy, 80, Amagar Boulevard, Copenhagen, on April 25. After the business meeting there will be a symposium on "The Treatment of Poliomyelitis Complications at the Acute Stage." Further information may be obtained from the secretariat general of the association, 130, Rue de Linthout, Bruxelles.

NEW ISSUES

Medical and Biological Illustration.—The next issue (Vol. 3, No. 1) will be available in a week's time. The contents include:

POST-MORTEM EXAMINATION OF THE CORONARY ARTERIES. Deryk Snow and Robert Ollerenshaw.
BOTANICAL ILLUSTRATION. Stella Ross-Craig.
MOUNTING: PART I. THE MOUNT AND THE ORIGINAL. Sylvia Treadgold.
PHOTOGRAPHY IN PLANT PEST AND DISEASE CONTROL. C. M. Cadwallader.
SOME CHARACTERISTICS OF EFFECTIVE TEACHING FILMS. L. P. Greenhill and C. R. Carpenter.
EQUIPMENT AND METHODS:
THE E.E.L. COLOUR TEMPERATURE METER.
THE ILFORD "SKYHOOK" LIGHTING SET.
AN AID TO SKETCHING.
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SOCIETIES AND LECTURES

Details in this column are necessarily brief. Further information and tickets where required (marked ●) should be obtained from the institution concerned.

Monday, March 16

MEDICAL SOCIETY OF LONDON.—8.30 p.m., Lettsomian Lecture by Dr. E. R. Cullinan: Some Disorders of the Liver and Bile Passages.
ROYAL EYE HOSPITAL.—5.15 p.m., Dr. T. H. Whittington: Science and Art of Refraction—Introduction.

Tuesday, March 17

CAERNARVONSHIRE AND ANGLESEY PAEDIATRIC CLUB.—At Clinic, Sackville Road, Bangor, 4.30 p.m., Dr. Alice M. Stewart: The Relation Between the Health of the Newborn and the Health of the Mother.
●INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. F. R. Bettley: Antibiotics.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Hunterian Lecture by Professor D. MacG. Jackson: Treatment of Burns—an Exercise in Emergency Surgery.
SOUTH-WEST LONDON MEDICAL SOCIETY.—At Bolingbroke Hospital, S.W., 8.30 p.m., Mr. Douglas MacLeod: Some Causes of Pelvic Pain in Women.
WEST END HOSPITAL FOR NERVOUS DISEASES.—5.30 p.m., Mr. I. R. McCaul: Investigation of Cerebral Tumour.

Wednesday, March 18

CHARTERED SOCIETY OF PHYSIOTHERAPY: TAUNTON AND DISTRICT BRANCH.—At Musgrove Park Hospital, Taunton, 8 p.m., Professor R. Milnes Walker: Cardiac Surgery.
●INSTITUTE OF DERMATOLOGY.—5.30 p.m., Dr. H. Haber: Keratoses and Keratodermias.
INSTITUTE OF UROLOGY.—At St. Paul's Hospital, W.C., 4.30 for 5 p.m. Mr. A. W. Badenoch: Haematuria.
LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE.—4 p.m., Dr. C. C. Chesterman: The Training of Auxiliary African Medical Personnel.
MIDLAND MEDICAL SOCIETY.—At Birmingham Medical Institute, 8.15 p.m., Professor J. M. Webster: Medical and Legal Aspects of Criminal Abortion.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—4 p.m., annual general meeting of Faculty of Anaesthetists; 5 p.m., Joseph Clover Lecture by Professor E. A. Pask: James Brown.
ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE.—3.30 p.m., Dr. J. A. Scott: Contribution of the Health Centre to the Public Health.

Thursday, March 19

BRITISH INSTITUTE OF RADIOLOGY.—8 p.m., Professor Olle Olsson (Sweden): Some Roentgendiagnostic Problems Connected with Bright's Disease.
EDINBURGH CLINICAL CLUB.—At B.M.A. Scottish House, 8 p.m., Dr. I. R. C. Batchelor: Alcoholism.
LIVERPOOL MEDICAL INSTITUTION.—At Sefton General Hospital, 2.30 p.m., afternoon clinical demonstration.
ROYAL COLLEGE OF SURGEONS OF ENGLAND.—5 p.m., Hunterian Lecture by Professor G. K. Tutton: Cerebral Abscess—The Present Position.
ROYAL EYE HOSPITAL.—5.30 p.m., Miss M. Savory: Eye Surgery in the Elderly and Infirm.
ROYAL SOCIETY OF TROPICAL MEDICINE AND HYGIENE.—At Royal Army Medical College, 7.30 p.m., laboratory meeting.

Friday, March 20

BRITISH INSTITUTE OF RADIOLOGY.—5 p.m., meeting of Medical Members; 6.30 p.m., Dr. L. F. Lamerton, M.Sc., Ph.D.: Study of the Phases of Radiation Response in the Rat.
FACULTY OF RADIOLOGISTS.—At Royal College of Surgeons of England, 2 p.m., Admission of Fellows; 2.30 p.m., Dr. A. G. Morrow: Percutaneous Portal Venography and its Surgical Application; Dr. I. B. D. Middlemass: Deformity of Oesophagus in Bronchogenic Carcinoma; Dr. N. N. Blaxland: Vacuum Phenomenon in the Spine; Dr. L. L. Ralph: Internal Carotid Thrombosis.
●INSTITUTE OF DERMATOLOGY.—5.30 p.m., clinical demonstration by Dr. R. M. B. MacKenna: Local Treatment.
OSLER CLUB OF LONDON.—At 11, Chandos Street, W., 7.45 p.m., Dr. W. R. Bett: History, Folk-lore, and Anthropology of Enuresis. Discussion by Dr. R. Sessions Hodge and Dr. C. Hooykaas.
ST. GEORGE'S HOSPITAL MEDICAL SCHOOL.—5.30 p.m., Jenner Memorial Lecture by Dr. R. Lewthwaite: Preventive and Therapeutic Aspects of the Typhus Group of Fevers
SOCIETY OF PUBLIC ANALYSTS: PHYSICAL METHODS GROUP.—At King's College, Strand, W.C., 2.20 p.m., Symposium: Developments in Microscopical Methods.

APPOINTMENTS

MANCHESTER REGIONAL HOSPITAL BOARD.—J. Cowan, M.B., Ch.B., D.M.R.D., Consultant Radiologist to Crumpsall, Monsall, and Booth Hall Hospitals, Manchester; B Boas, M.D., Assistant Ophthalmologist to Ashton-under-Lyne General Hospital and to Lancashire, Cheshire, and Derbyshire Local Authorities; M. R. Geake, M.B., B.Chir., M.R.C.P., Consultant Chest Physician, Preston and Chorley Hospital Centre; J. A. L. Cooper, M.R.C.S., L.R.C.P., D.A., Consultant Anaesthetist to Preston and Chorley Hospitals; N. W. Gill, M.B., B.S., F.R.C.S., Consultant Ear, Nose, and Throat Surgeon to South Manchester Hospitals; A. Jolleys, M.D., F.R.C.S., Consultant Paediatric Surgeon to Royal Manchester Children's and Booth Hall Hospitals; F. A. L. Da Cunha, M.B., B.Chir., M.R.C.O.G., Assistant Consultant Obstetrician/Gynaecologist to Oldham and Ashton Hospitals; R. H. Seville, M.D., M.R.C.P., Consultant Dermatologist to Lancaster, Barrow, and Blackpool Hospital Centres; T. F. McCarthy, M.D., M.R.C.P.Ed., Assistant Physician, Nab Top Sanatorium, Marple, A. B. Colohan, M.B., B.Ch., Tuberculosis Physician and Medical Officer in Charge of Mass Miniature Radiography Unit based at Chorley; Hildegard C. Fisher, M.D., D.P.M., Assistant Psychiatrist, Lancaster Moor Hospital; N. E. Rankin, M.B., B.S., Assistant Pathologist to Bury and Rossendale Hospital Centre; I. S. Mudie, M.B., Ch.B., D.T.M.&H., Tuberculosis Physician to Altrincham, Mid-Cheshire, and Crewe Areas.

O'CONNOR, M. C., M.B., B.S., Temporary Medical Officer of Health, Long Ashton Rural District, Bristol.

TODD, ELZA HARRIS, M.B., Ch.B., D.P.H., Assistant Medical Officer, Area 9 (Heston, Isleworth, Southall, Brentford and Chiswick), Middlesex County Council.

BIRTHS, MARRIAGES, AND DEATHS

BIRTHS

Abramson.—On February 27, 1953, at the Ayrshire Central Hospital, to Dr. Morag (formerly Dods), wife of Dr. Allan Abramson, a daughter.
Crow.—On March 2 1953, at the Kingston Hospital, to Barbara (formerly Killick), M.B., Ch.B., D.C.H wife of Robert S. Crow, M.B., Ch.B., M.R.C.P., of 8, Brunswick Road, Kingston-on-Thames, Surrey, a son.
McGowan.—On March 4, 1953, at 2, Stoke Paddock Road, Bristol, to Rosalind (formerly Barclay), wife of Dr. G. K. McGowan, a daughter.
MacTaggart.—On March 2, 1953, to June Mary, M.B., Ch.B., D.P.H., wife of Douglas Keith MacTaggart, M.B., Ch.B., D.P.H., of Springfield, Culcheth, Warrington, Lancs, a son.
Pack.—On March 3, 1953, to Dr. Mary Pack (formerly Stanton), wife of Dr. Gordon Pack, of Andover, Hants, a son—Andrew Gordon.
Warin.—On February 22, 1953, at the Maternity Hospital, Bristol, to Anne, wife of Dr. R. P Warin, a daughter.
Wilkinson.—On February 25, 1953, at the Queen Mary Hospital, Stratford, London, E., to Patricia, wife of Dr. Harry Wilkinson, a son.

MARRIAGES

Polwin—Barkway.—On March 7, 1953, at St. John's Church, Buckhurst Hill, Essex, Stephen J. S. Polwin, M.B., B.Ch., D.Obst.R.C.O.G., to Dorothy Margaret Barkway.

GOLDEN WEDDING

Primmer—Robertson.—On March 10, 1903, John Boyd Primmer, M.B., Ch.B., to Jean Robertson, of Dunfermline, now of Aberdour, Fifeshire.

DEATHS

Cuff.—On February 15, 1953, at St. Stephen's Hospital, Barnet, Herts, Sidney Wilmot Cuff, L.M.S.S.A.
Forssander.—On February 14, 1953, Dorothy Jean Ogilvie Forssander (formerly Dinnick, née Mitchell), L.R.C.P.&S.Ed., L.R.F.P.S., L.D.S. R.C.S.Ed., of Victoria, British Columbia, Canada.
Griffin.—On February 14, 1953, James Valentine Griffin, L.R.C.P.&S.I. & L.M., of The New House, Goldsmith's Avenue, Crowborough, Sussex, aged 82.
Hill.—On February 15, 1953, John Percival Hill, M.D., of The Limes, Stowmarket, Suffolk, aged 79.
Hunter.—On February 27, 1953, at Wakefield, Evelyn Margaret Hunter, wife of John Hunter, M.B., Ch.B., D.P.H., of 60, Batley Road, Wakefield, Yorks.
Hutton.—On February 16, 1953, in a nursing-home, Leeds, Albert Edward Hutton, M.R.C.S., L.R.C.P., of 4, The Grange, Far Headingley, Leeds, aged 81.
Johnstone.—On February 14, 1953, at the West London Hospital, James Johnstone, M.B., F.R.C.S., D.P.H., J.P., of Richmond, Surrey, aged 90.
Nelson.—On February 17, 1953, at "Beechwood," Beech Lane, Calderstones, Liverpool, Philip Nelson, M.D., Ph.D.
Sandeman.—On February 20, 1953, at Kevin, Bridge-of-Weir, Renfrewshire, Walter Sandeman, M.B., C.M., D.P.H., aged 92.
Walker.—On February 17, 1953, at Churchill Court, near Bristol, John William Walker, O.B.E., F.R.C.S., aged 93.

Any Questions?

Correspondents should give their names and addresses (not for publication) and include all relevant details in their questions, which should be typed. We publish here a selection of those questions and answers which seem to be of general interest.

B.C.G. in Infancy

Q.—*What is the best age for inoculating infants with B.C.G.? Are there any special dangers from doing this at too early an age?*

A.—There is no reason why an infant should not be vaccinated with B.C.G. within a few hours of birth. As the infant has to be segregated from all risk of tuberculous infection until conversion has occurred, the later the vaccination is left the greater will be the problem of segregation. The usual practice is to vaccinate as soon as the infant has regained its birth weight.

There are no dangers from vaccinating an infant at too early an age. The glandular complications which sometimes arise after B.C.G. nearly all occur in infants vaccinated during the first two years of life—particularly if the vaccination is done on the thigh. There is no evidence to suggest that they are any more frequent in infants vaccinated at birth.

Treatment of Impetigo

Q.—*What is the best treatment for impetigo nowadays?*

A.—Among effective applications in the treatment of impetigo are 2% hydrarg. ammon. in Lassar's paste, copper and zinc sulphate lotion (*N.F.*) used with equal parts of hot water, and the aniline dyes in lotion, cream, or paste. If there is much exudation the dyes in lotion form may cause trouble by forming scabs which dam back infected exudate. Deliberate removal of scabs and vigorous cleansing or interference are usually undesirable and unnecessary.

Sulphonamides and antibiotics should not be employed as local applications. Provided the organisms are sensitive, these remedies may be used systemically as for other pyogenic infections if the circumstances, site, or severity of the affection justify this course, as, for instance, in impetigo neonatorum, impetigo of scalp or beard in the adult male, etc. For these cases a small dosage, such as sulphathiazole, 0.5 g. four times a day for seven days, is adequate; in addition bland local applications like zinc paste or calamine may be employed.

A search for the source of infection and its treatment, and precautions to prevent repeated auto-inoculation or the infection of others, are also necessary.

Anticoagulant Therapy and Coronary Infarction

Q.—*What effect has ethyl biscoumacetate ("tromexan") on an established case of coronary infarction? Is it worth a trial, and should the patient be treated in hospital?*

A.—Anticoagulant treatment as such can have no effect on an established cardiac infarct. If the question means, "Has ethyl biscoumacetate any effect on angina pectoris following cardiac infarction?" then the answer is probably no, in the sense that attacks of pain on effort are unlikely to be influenced, although it is admitted that both heparin and dicoumarol are weak coronary vasodilators, and it is possible that ethyl biscoumacetate is also. If the question is, "Has ethyl biscoumacetate any value in discouraging further attacks of coronary thrombosis?" then the answer is yes, but this means permanent biscoumacetate therapy, or an occasional six weeks' course of therapy when the patient's condition suddenly deteriorates (acute coronary insufficiency). If ethyl biscoumacetate is given within the first few days of such deterioration, it is probable that coronary thrombosis or a serious extension of a thrombosis already present can be prevented. In any individual case one has to judge whether conditions will be favourable for permanent biscoumacetate therapy, and whether the patient will accept with equanimity a weekly blood test for the rest of his life. In this country permanent biscoumacetate therapy is rarely used, but there is undoubtedly a case for it in certain instances, particularly when recurring thromboses, not necessarily confined to the coronary arteries, are evident, and when it has been demonstrated that a relatively stable prothrombin time can be achieved with a fixed daily dose. The patient should be warned that his reaction to the drug may alter seriously as the result of any intercurrent illness.

Baldness in Women

Q.—*(1) Does the hereditary factor in baldness express itself in women, and, if so, in what way? For instance, are the daughters of a bald father especially prone to baldness? (2) What is the best treatment for thinning of the hair in women?*

A.—(1) Although the hereditary factor in calvities in women is well known, it is not, in my experience, a very important influence. It is quite unusual for women with this complaint to give a family history, and I think it unlikely that the daughters of a bald father are more susceptible to calvities than other women. However, I do not know of any careful statistical survey.

(2) It is doubtful how much calvities can be influenced by treatment. In practice usually the best that can be done is to give a mild stimulating lotion to be used once or twice a day for an indefinite period. A suitable lotion is salicylic acid and mercuric chloride lotion (*N.F.*).

Dangers of Aluminium Welding

Q.—*I have been asked to advise a local firm who are setting up a workshop where some 30 men will be doing more or less continuous aluminium welding. Are there any particular dangers associated with this, and, if so, how can they be prevented? I will also be asked to examine these welders before their employment. Are there any conditions which should exclude them from this work, and do you advise chest radiography?*

A.—The welding of aluminium has been done for only about eight years, but the practice is increasing. It may be done either by the oxyacetylene or by the electric-arc method. The aluminium both in the "parent" metal and the electrodes may be alloyed with other metals such as copper, nickel, manganese, zinc, and lead. The risk to health will vary according to the composition and concentration of the fumes and gases coming off the welding operation; these in turn vary with the types of electrodes used and the current strength. The oxyacetylene method produces more nitrous oxides and ozone than the electric arc (particularly the "shielded arc"), and one case of oedema of the lungs has been reported in a man who was doing oxyacetylene welding of aluminium in a confined space. A typical analysis of the fumes of aluminium welding shows 35.6% Al_2O_3, 2.9% MgO, 6.5% fluorine, and 23.7% chlorine. Metal-fume fever might be caused by inhalation of the freshly formed metallic oxides, but the greatest risk is that of gassing with the nitrous oxides and/or ozone if the work is done in a confined space. Prevention is best secured by local exhaust ventilation over each welding point, even when the work is done in an open shop. Pre-employment and periodical examinations, with *x*-ray examination of the chest, are always useful. The *x*-ray film is good documentary evidence of inhalation of the metallic

oxides, and after 10 years or so of welding might show abnormal shadows simply because these oxides are opaque to *x* rays. There is some controversy about the effects of aluminium and its oxides on the lungs; some reports say that they are harmless, others that they cause fibrosis or granulomata of the lungs. Animal experiments have shown that hydrated alumina, for instance, increases the susceptibility of the animals to tuberculosis. Any man who has a pulmonary condition such as quiescent or active tuberculosis, chronic bronchitis, emphysema, or asthma should not be allowed to do aluminium welding.

Asthma in the Bride

Q.—*A young woman of 22 has had typical symptoms of hay fever, when exposed to horse, cat, and dog fur, from the age of 14 years. The symptoms are now largely controlled as the result of specific desensitization, but she has had typical mild asthmatic attacks for the last 18 months. She is shortly to be married, and her fiancé also suffers from seasonal hay fever. What prognosis can be given for her asthma, and are the children of the marriage bound to suffer from hay fever or asthma? She is intelligent and happy and has a well-balanced personality.*

A.—An investigation of the cause of the asthma for the last 18 months should be carried out. The patient is obviously an allergic person and a new sensitivity may have developed. A psychological or an infective cause appears unlikely from the history. The prognosis would obviously be considerably improved if the cause could be found, and she might, by investigation and proper advice now, furnish her new home so as to exclude or reduce to a minimum the present cause of her attacks.

The prognosis over the next ten years or so should be quite good, even if the cause is not found. Most young asthmatics are much improved during pregnancy, but some become somewhat worse afterwards: avoidance of getting overtired and developing a superadded infection will reduce this tendency to a certain extent. The children are not bound to suffer from asthma or hay fever, but they will have an increased tendency to do so. There is little published work on the risks to children of allergic parents, but it would appear that the risk of the children in this case having a major allergic manifestation would be 20–25%.

Massive Doses of Vitamin D

Q.—*What are the therapeutic advantages of massive doses of vitamin D over ordinary amounts? A child of 10 years has been recommended 500,000 international units at fortnightly intervals. Is this safe?*

A.—In the prevention and treatment of rickets massive doses of vitamin D may be useful in times of famine or in other situations where there is little chance that the infant will receive regular supervision and adequate medical care. A single dose of 300,000 international units may be given by mouth with reasonable safety and for its curative effects. Under normal circumstances, however, a small daily dose of cod-liver oil or halibut-liver oil (providing 400–800 international units for prevention of rickets, or about 3,000 international units for treatment) is to be preferred.

The second part of this question is difficult to answer without knowing why a child of 10 years has been recommended a therapeutic dose of vitamin D. If the child is in normal health it should not require any supplement of vitamin D at the age of 10. There are only three extremely rare conditions in which a child of this age might require large doses of the vitamin: vitamin D-resistant rickets (DRR), "renal rickets," or lupus vulgaris. In the last condition it is usual to give vitamin D daily by mouth beginning with a dose of 50,000 units and increasing to 150,000 units. Careful supervision is needed to avoid the danger of overdosage, which may be heralded by loss of appetite, nausea, and weakness; the blood urea and serum calcium may become elevated. If overdosage is continued, calcification may develop in the kidneys and arteries. There are no other indications for prescribing large amounts of vitamin D. Because of the danger of overdosage, it is certainly not a safe procedure in the absence of careful supervision.

What Can be Mixed with Penicillin?

Q.—*What drugs and sera can be safely mixed in the same syringe with crystalline penicillin? Can A.T.S., morphine, atropine, pethidine, and aminophylline be used in this way?*

A.—Crystalline penicillin is fairly stable at a *p*H of about 6–6.5, and it can be mixed in a syringe with A.T.S., morphine sulphate, atropine sulphate, pethidine, and aminophylline without causing any immediate precipitation. It should, however, be used at once, as a precipitate may form slowly with the alkaloids. Though it is sometimes convenient to give penicillin with A.T.S., there can be few occasions when it is desirable or in any way advantageous to combine penicillin in one single intramuscular injection with the other drugs mentioned above.

NOTES AND COMMENTS

Implantation of Hormone Pellets.—Mr. A. R. G. CHAMINGS, B.Pharm., Ph.C. (Ciba Laboratories), writes: The answer to the question on the sterilization of hormone implants (February 28, p. 519) includes the statement, "Should the pellet become contaminated it may be sterilized by boiling in water in a test-tube." We believe we should draw your attention to the fact that this procedure will soften the pellet even to the extent of complete disintegration and should not therefore be adopted. Similarly, autoclaving at 10 lb. per sq. in. (0.7 kg. per sq. cm.) for 30 minutes (*B.P.* method) cannot be used, as the hormone will melt. Hormone implants are manufactured by sterile processes, but if they should become contaminated they should be discarded.

OUR EXPERT writes: Before the war the pellets of steroid hormones supplied to me for implantation were not already sterilized by the makers as they are now, and on the instructions of the makers I regularly sterilized them by boiling in water for 5 to 10 minutes; they did not disintegrate. About two years ago I had occasion to re-sterilize a pellet, which I did by boiling, without any ill effect. On inquiry, I now find that this method is not applicable to all pellets.

Road Accidents.—Dr. J. F. BURDON (Paignton) writes: In "Any Questions?" (February 21, p. 466) under the title of "Road Accidents" your expert states that warm fluids such as tea should be given to patients suffering from the effects of such accidents. As gastric activity ceases for a time after a fright, and an anaesthetic may have to be given, it is surely undesirable to give anything by mouth to these cases.

Second Book of "Any Questions?"—A particularly useful chapter in the second book of *Any Questions?* is that on marital problems. Subjects discussed include the male climacteric, ejaculatio praecox, dyspareunia, contraception, and ovulation after delivery.

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